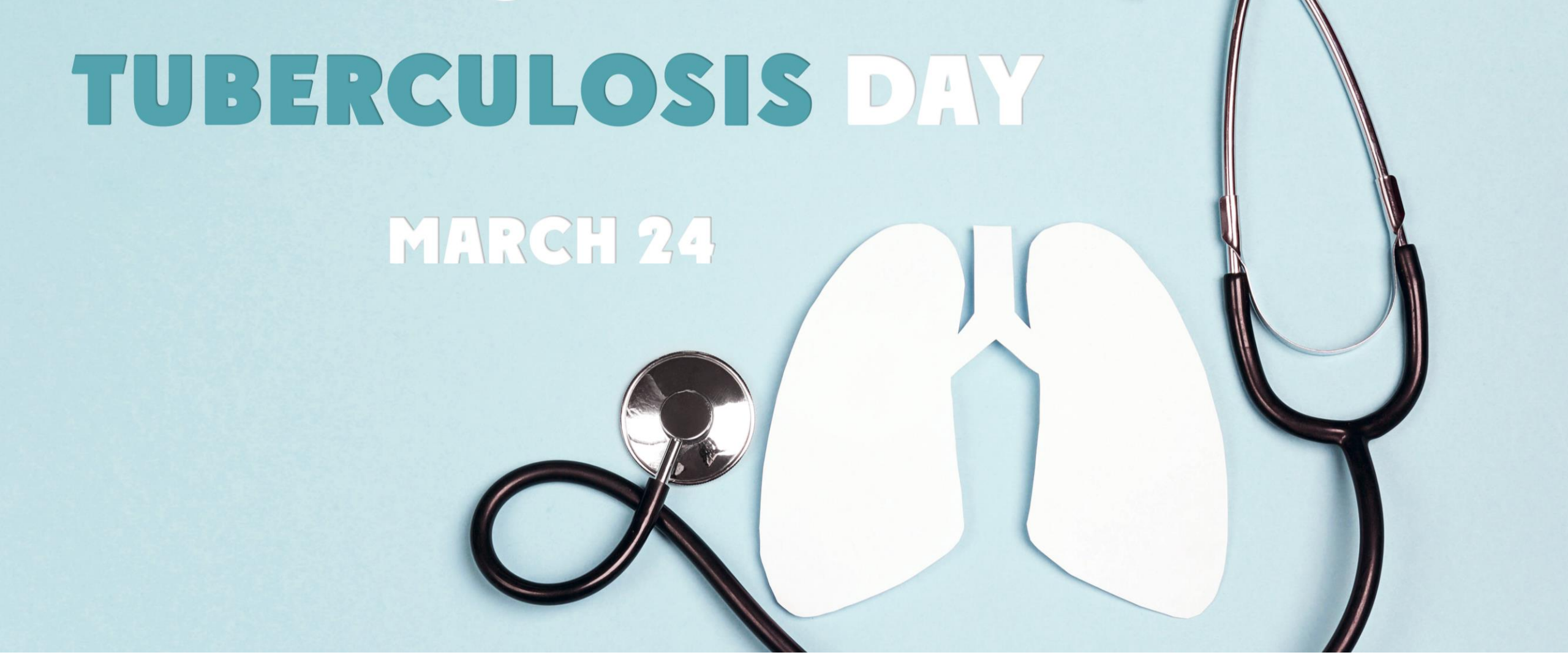



# ESSENTIAL COMPONENTS FOR ELIMINATION OF TUBERCULOSIS

Dee Pritschet, TB Prevention and Care Coordinator

North Dakota Department of Health

NORTH Dakota

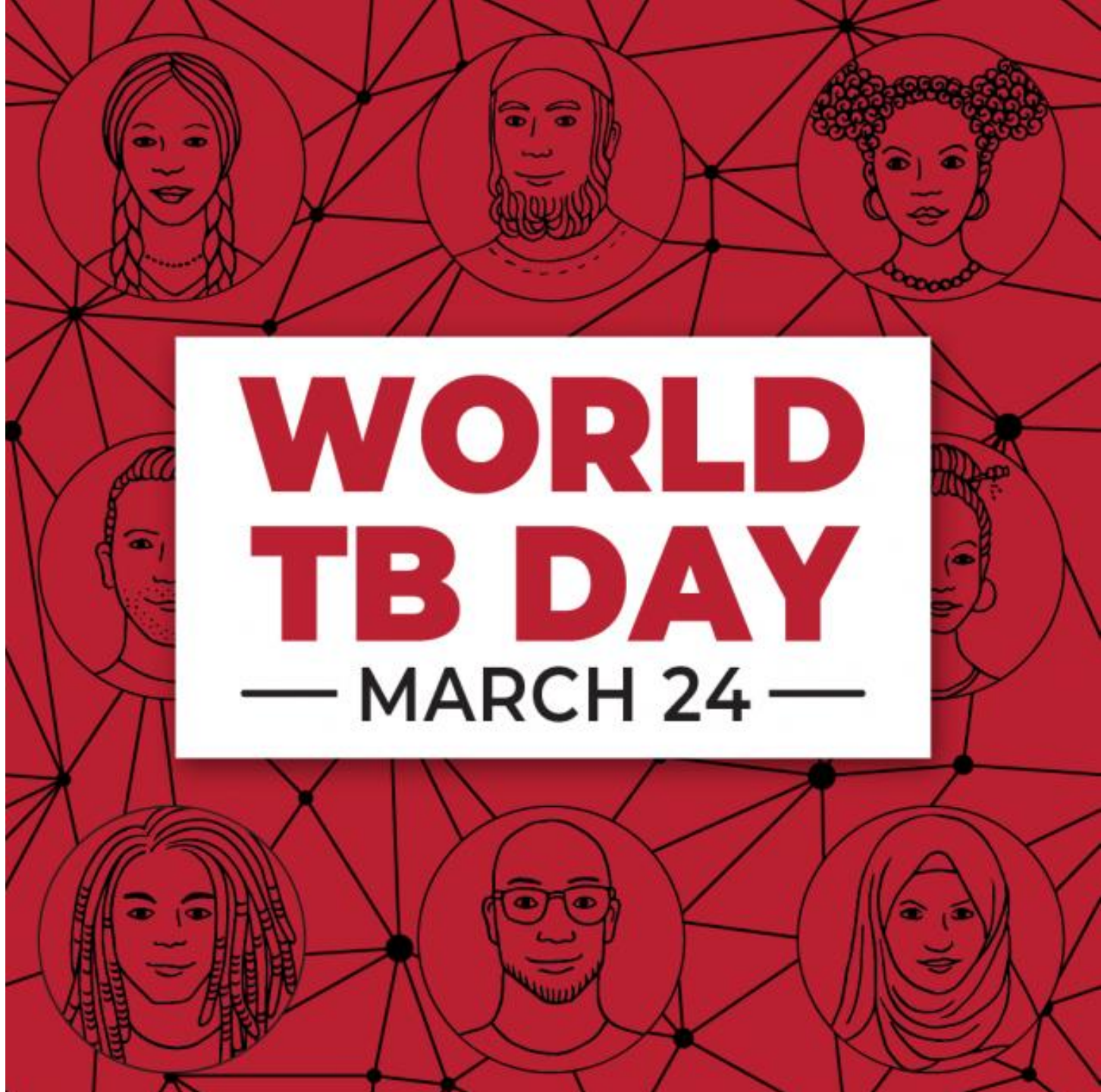
Be Legendary.™

# OBJECTIVES

- Discuss the overall approach, underlying principles and essential steps in implementing ending TB
- Explain North Dakota targets and indicators that can be used to monitor progress
- Review the TB Elimination Plan for North Dakota

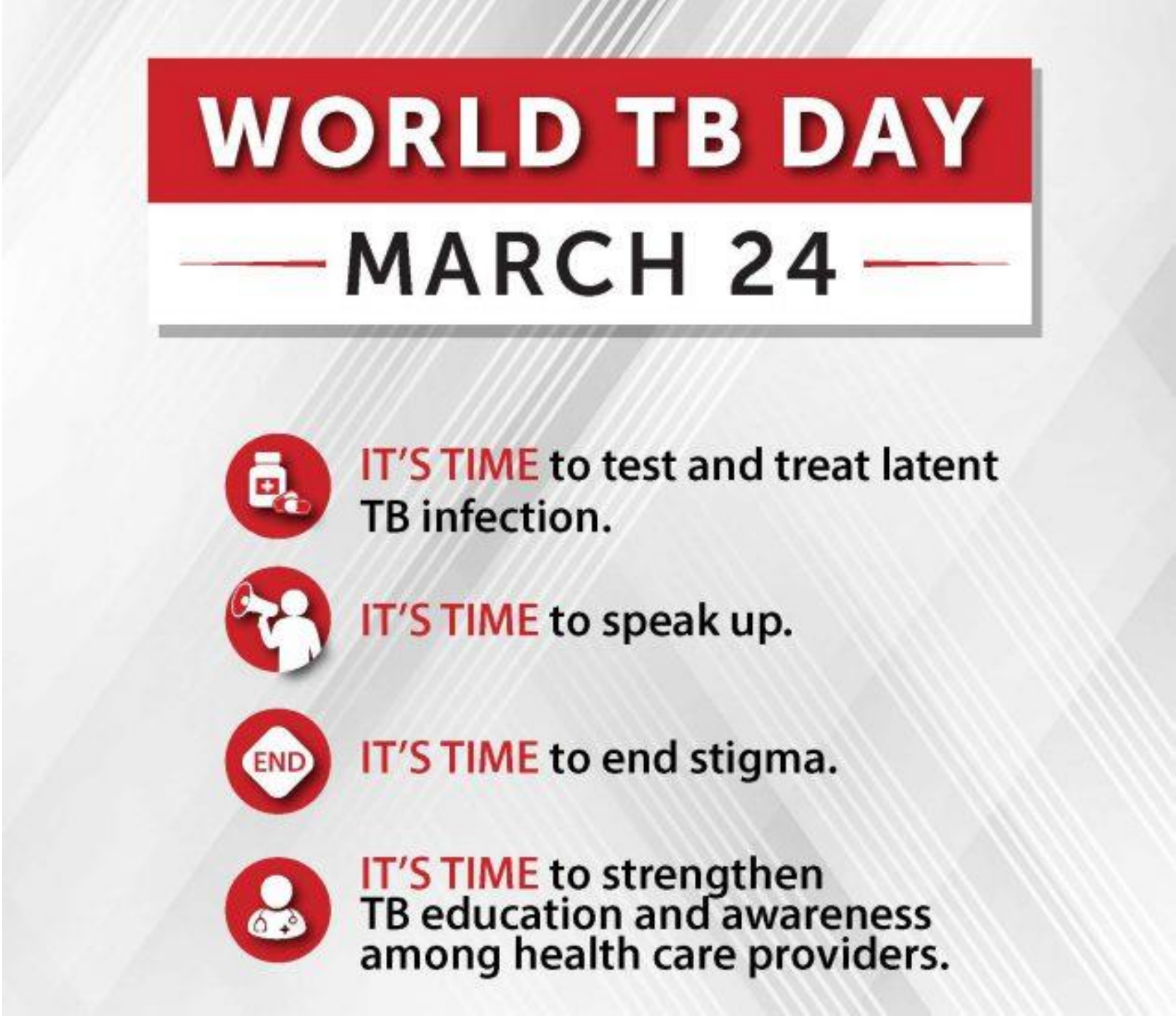
Each year, we commemorate World Tuberculosis (TB) Day on March 24 to raise public awareness about the devastating health, social and economic consequences of TB, and to step up efforts to end the global TB epidemic.

The date marks the day in 1882 when Dr. Robert Koch announced that he had discovered the bacterium that causes TB, which opened the way towards diagnosing and curing this disease.



# IT’S TIME

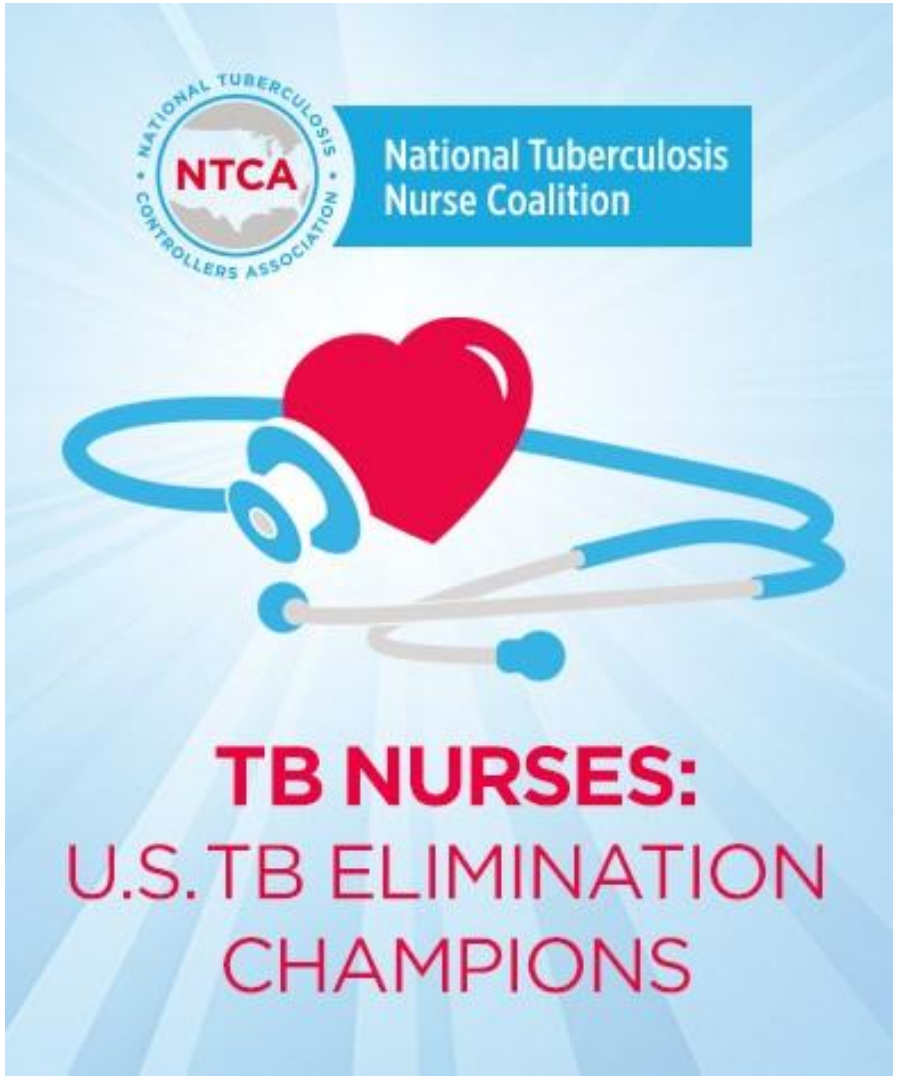
The spotlight this year is on urgently accelerating the TB response to save lives and end.



## THE NATIONAL TUBERCULOSIS CONTROLLERS ASSOCIATION WISHES TO RECOGNIZE ALL NURSES THAT CONTRIBUTED TO THE TB RESPONSE DURING COVID-19

Public health TB nurses provide care for patients in difficult and unknown circumstances.

During the COVID-19 pandemic, TB nurses use their case management skills to provide essential care and other related services for patients with COVID-19 and care for those with TB disease.



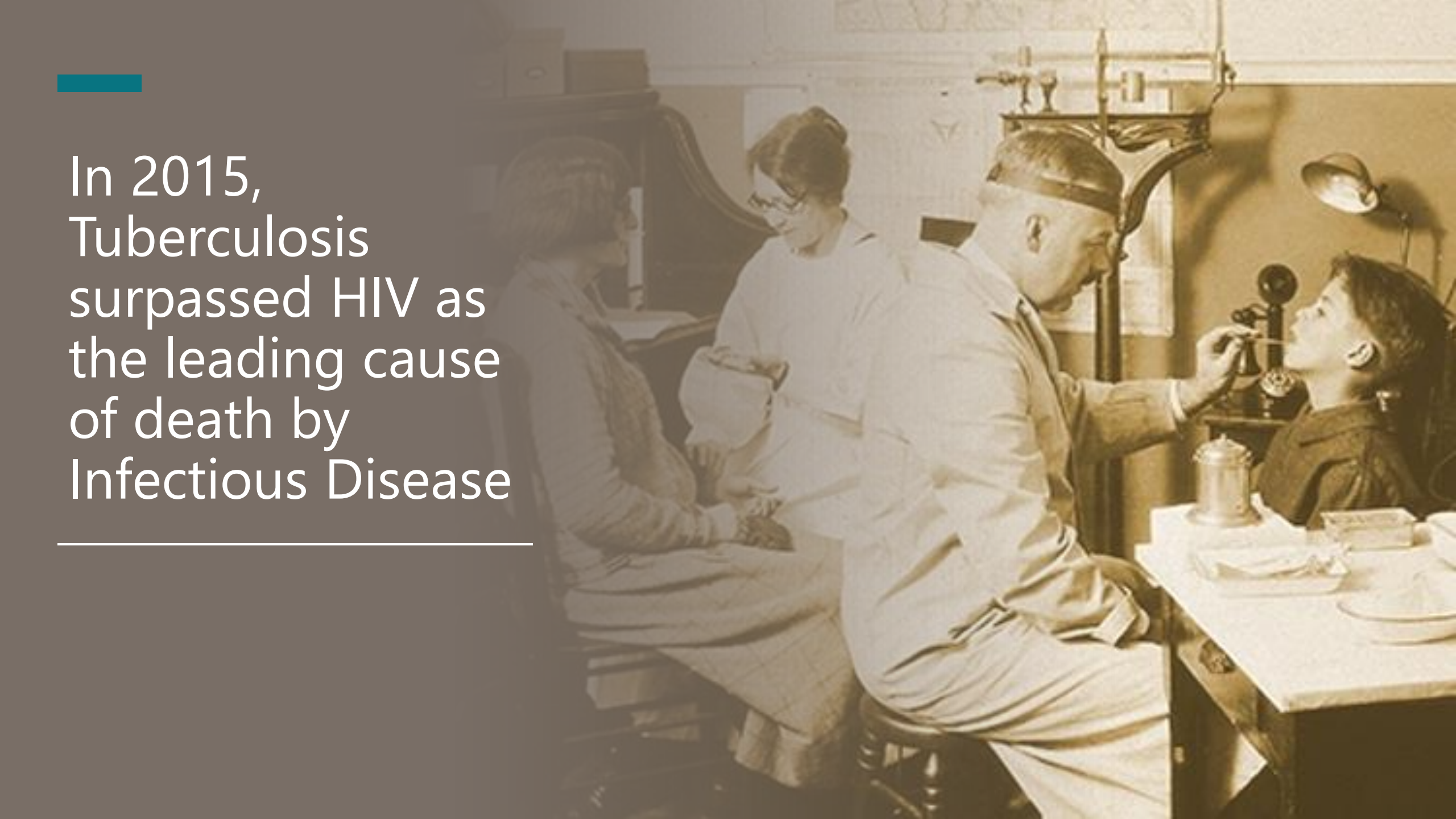
# Global Burden of Tuberculosis

# WHO GLOBAL TUBERCULOSIS REPORT 2020

| | Estimated Number of Cases | Estimated Number of Deaths |
|---|---|---|
| **All forms of TB** | 10 million | 1.4 million |
| **HIV-Associated TB** | 820,000 | 208,000 |
| **Multidrug-resistant TB (MDR-TB)** | 465,000 | ~150,000 |

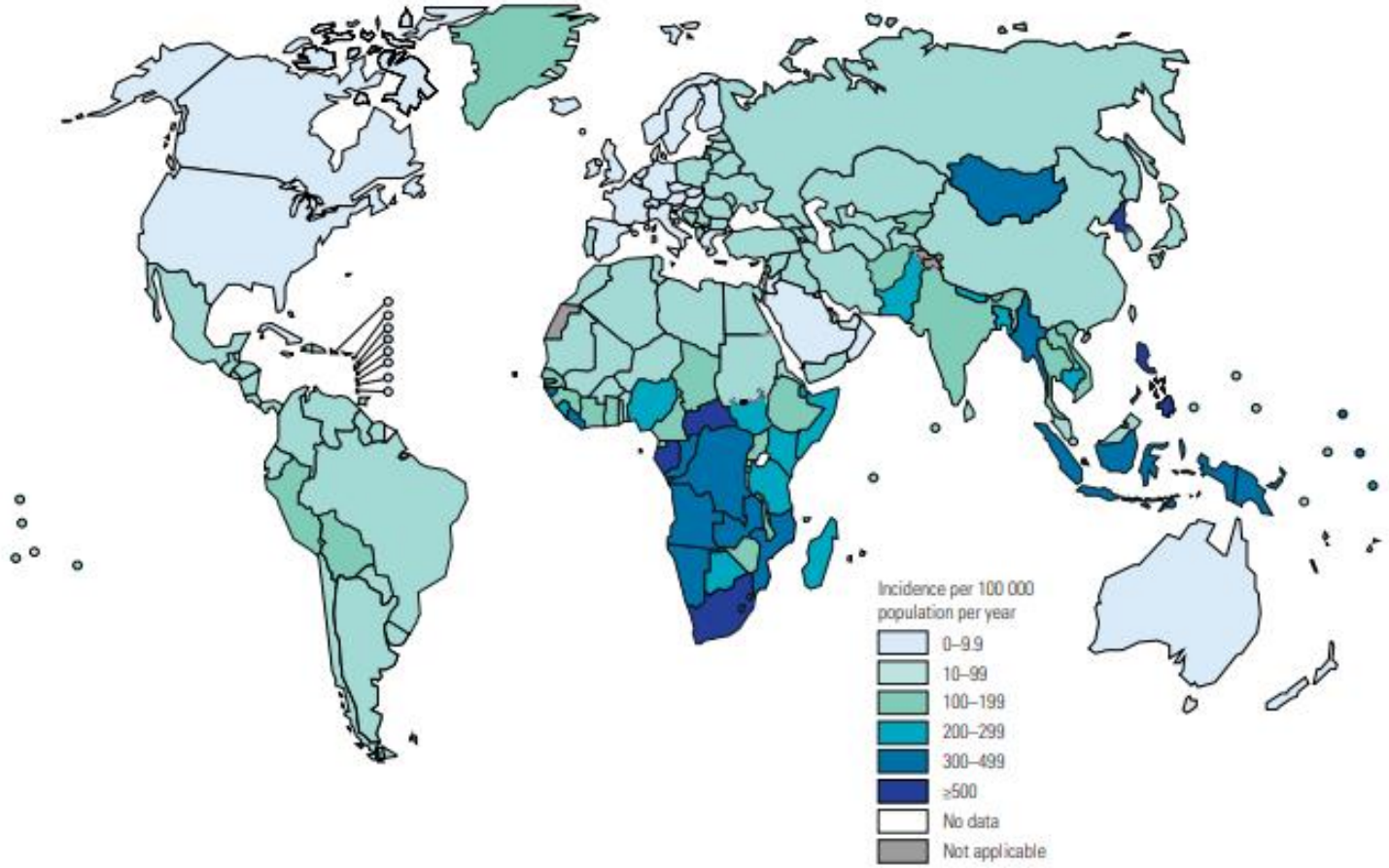
- Until 2020, TB was the world's deadliest infectious killer.
  - Each day, over 4000 people lose their lives to TB
  - Close to 30,000 people fall ill each day with this preventable and curable disease.
- Global efforts to combat TB have saved an estimated 58 million lives since the year 2000.

# In 2015, Tuberculosis surpassed HIV as the leading cause of death by Infectious Disease




Approximately 1/4 of the world
(1.95 billion) is infected with MTB

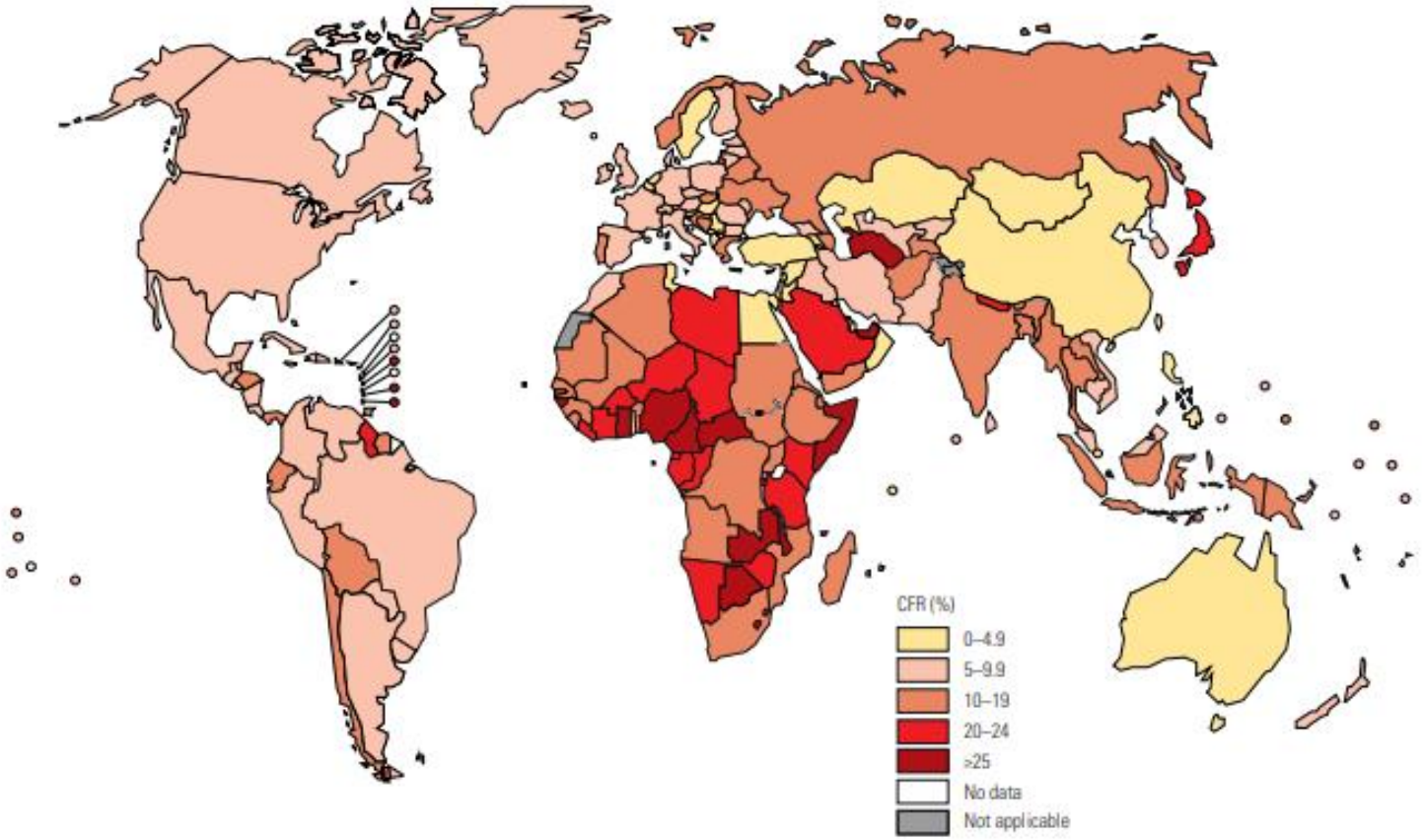
**Estimated TB incidence rates, 2019**



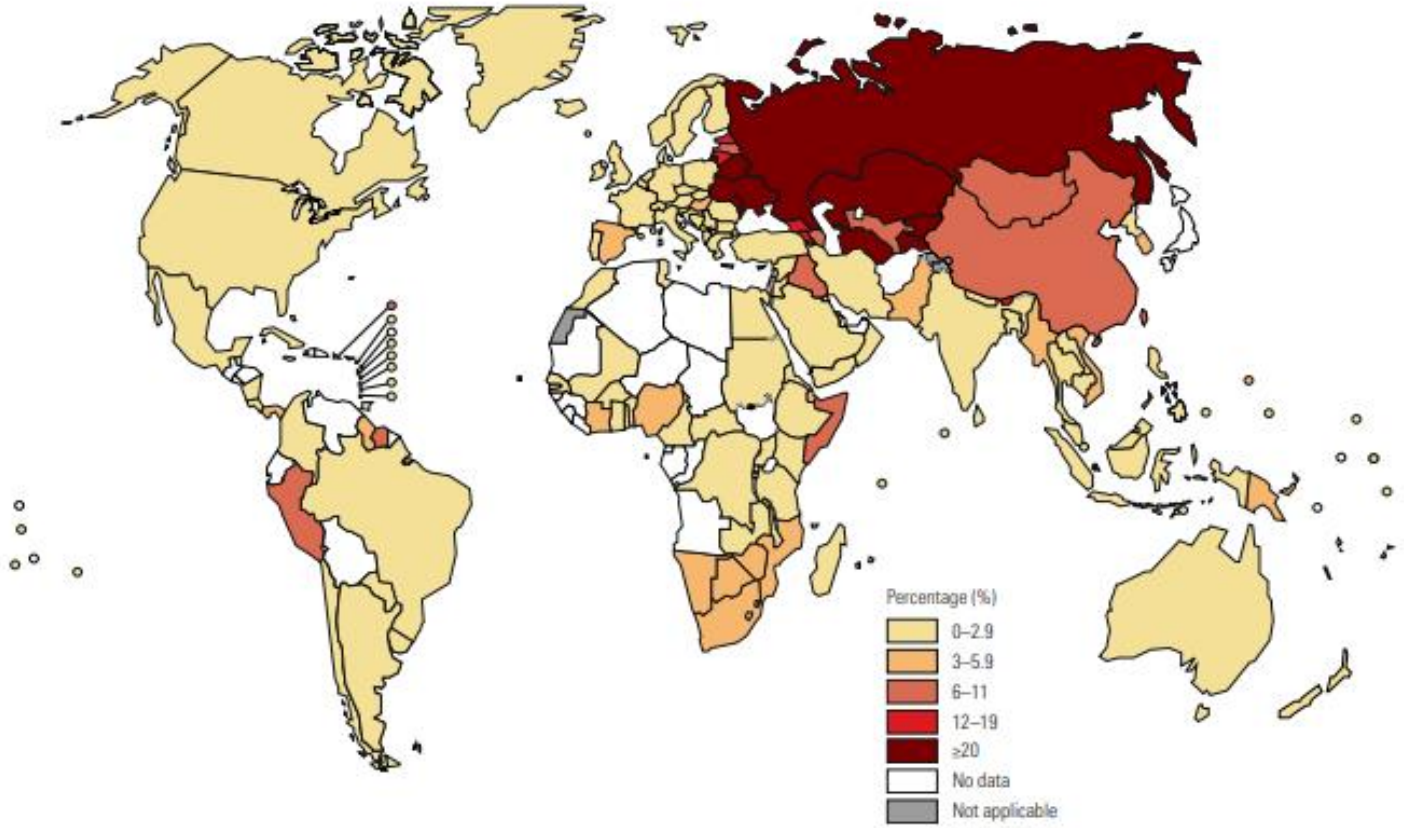
**Countries (in blue) that had an estimated TB incidence rate of less than 10 per 100 000 population in 2019**

[1] When an HIV-positive person dies from TB, the underlying cause is coded as HIV in the International Classification of Diseases system.

**Estimates of the case fatality ratio (CFR), including HIV-negative and HIV-positive people, 2019**



**Percentage of new TB cases with MDR/RR-TB[a]**

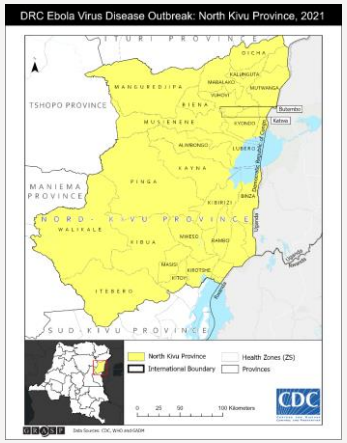



[a] Percentages are based on the most recent data point for countries with representative data from 2005 to 2020. Model-based estimates for countries without data are not shown. MDR-TB is a subset of RR-TB.

# THE COVID-19 PANDEMIC AND TB – IMPACT AND IMPLICATIONS GLOBALLY

- Two modelling analysis reached similar conclusions that TB numbers could rise to 2015 number or 2012 numbers
- Decrease case detection could lead to an additional 200,000 (2015) – 400,000 (2012) TB deaths
- Decreased access to TB treatment and TB preventative treatment

# Domestic Burden of Tuberculosis

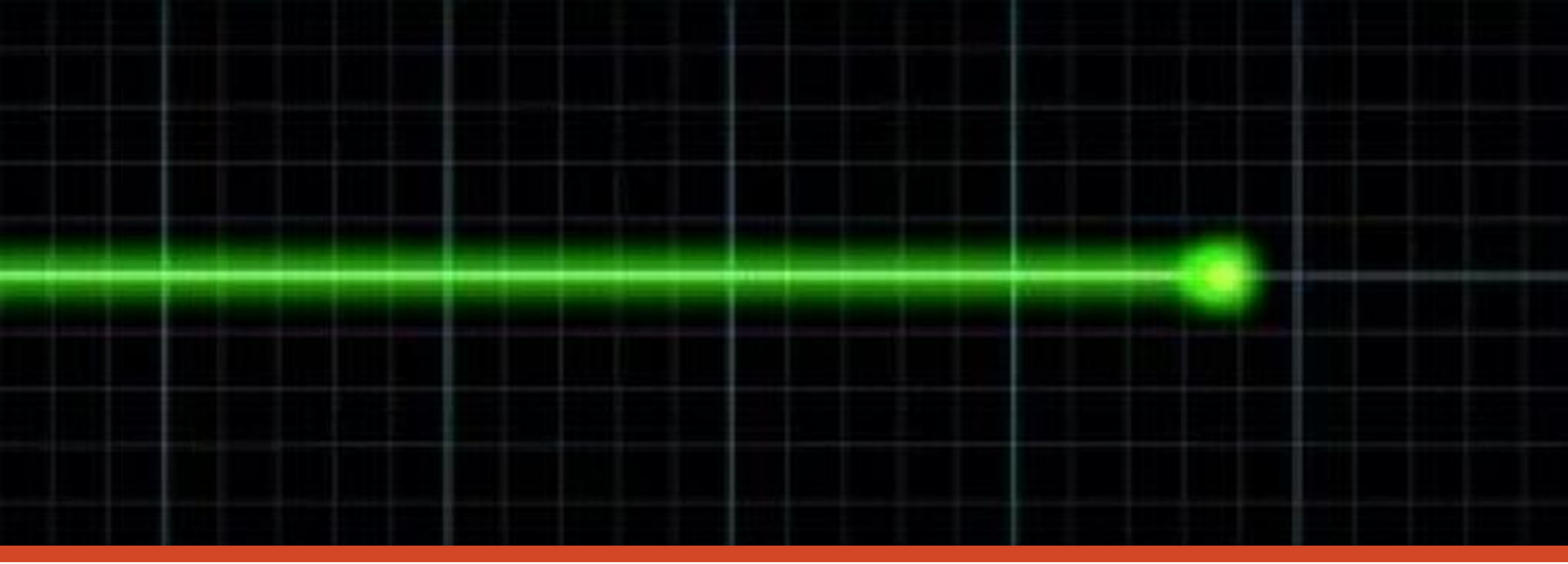

# Ebola or Tuberculosis

Which disease poses a greater risk to the US?

# US Response

In 2014 - $2 billion for Ebola

In 2016 – $1.8 billion for Zika



# Funding to the CDC for Domestic TB has been stagnant for the past 10 years

| Issue | Tuberculosis | COVID-19 |
|---|---|---|
| **History** | >70,000 years | Since December 2019 |
| **Mortality** | 1.4 M in 2019 | 2.4M on 19th Feb 2021 |
| **Transmission** | Aerosols | Mainly droplets, fomites, aerosols |
| **Infection Prevention** | Airborne infection control (administrative, environmental and respiratory protection) | Physical Distancing/Lockdown, hand hygiene, cough etiquette, disinfecting surfaces, face masks |
| **Active case finding** | Contact tracing, screening of risk groups | Contact tracing |
| **Diagnosis** | Molecular test-GeneXpert, TrueNat | 951 tests with 394 molecular test and ARDT by 24th Nov, 2020 |
| **Therapeutic** | 2 new drugs in the last 40-50 years | Over 700 drugs in pipeline, 70% in pre-clinical stage |
| **Vaccine** | No, BCG (100 yrs), M 72 | Pfizer/BioNTech, Moderna, Sinovac, Oxford Astrazeneca, Sinopharm, 69 vaccines in clinical development, 181-pre-clinical (WHO) |
| **Funding/economic impact** | 6.5 billion in 2019 | $ 14 trillion USD as of December 2020 (IMF Fiscal monitor report, Jan 2021) |
| **Political commitment** | Slow | +++ |

Global Funding

Source: Adapted from "New diseases and old threats: lessons from tuberculosis for the COVID-19 response" INT J TUBERC LUNG DIS 24(5): 2020 The Union

# TB Test Accuracy

## Sensitivity

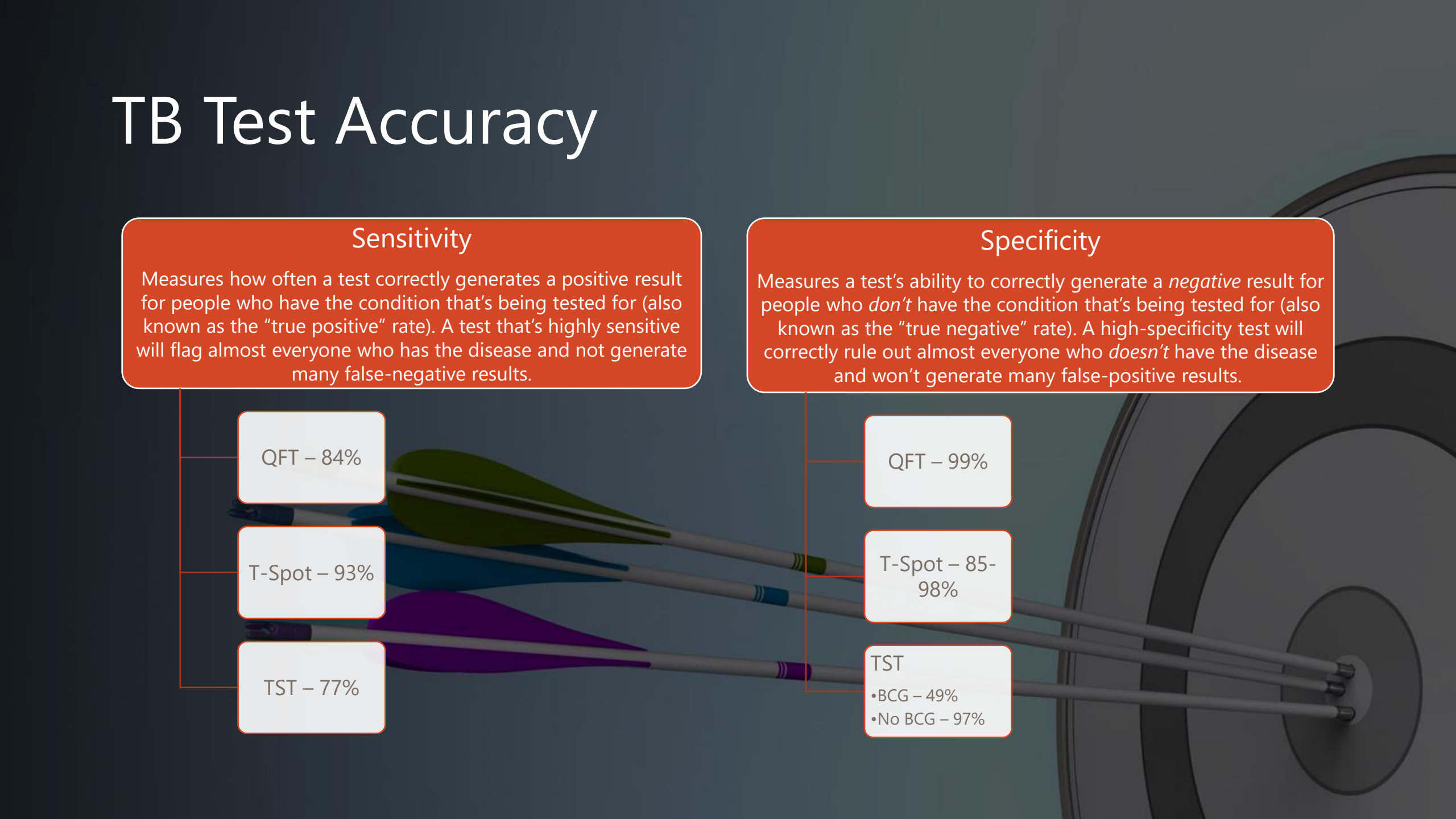
Measures how often a test correctly generates a positive result for people who have the condition that's being tested for (also known as the "true positive" rate). A test that's highly sensitive will flag almost everyone who has the disease and not generate many false-negative results.

- QFT – 84%
- T-Spot – 93%
- TST – 77%

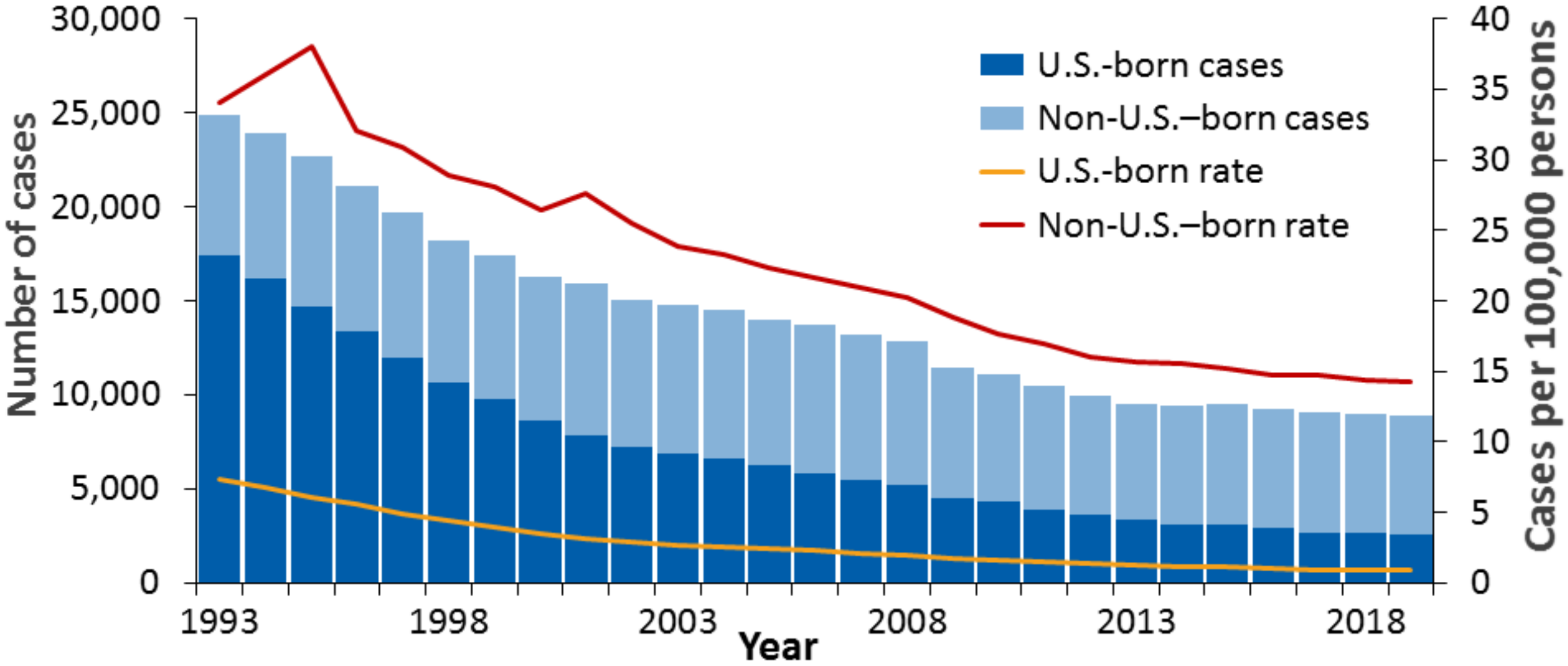
## Specificity

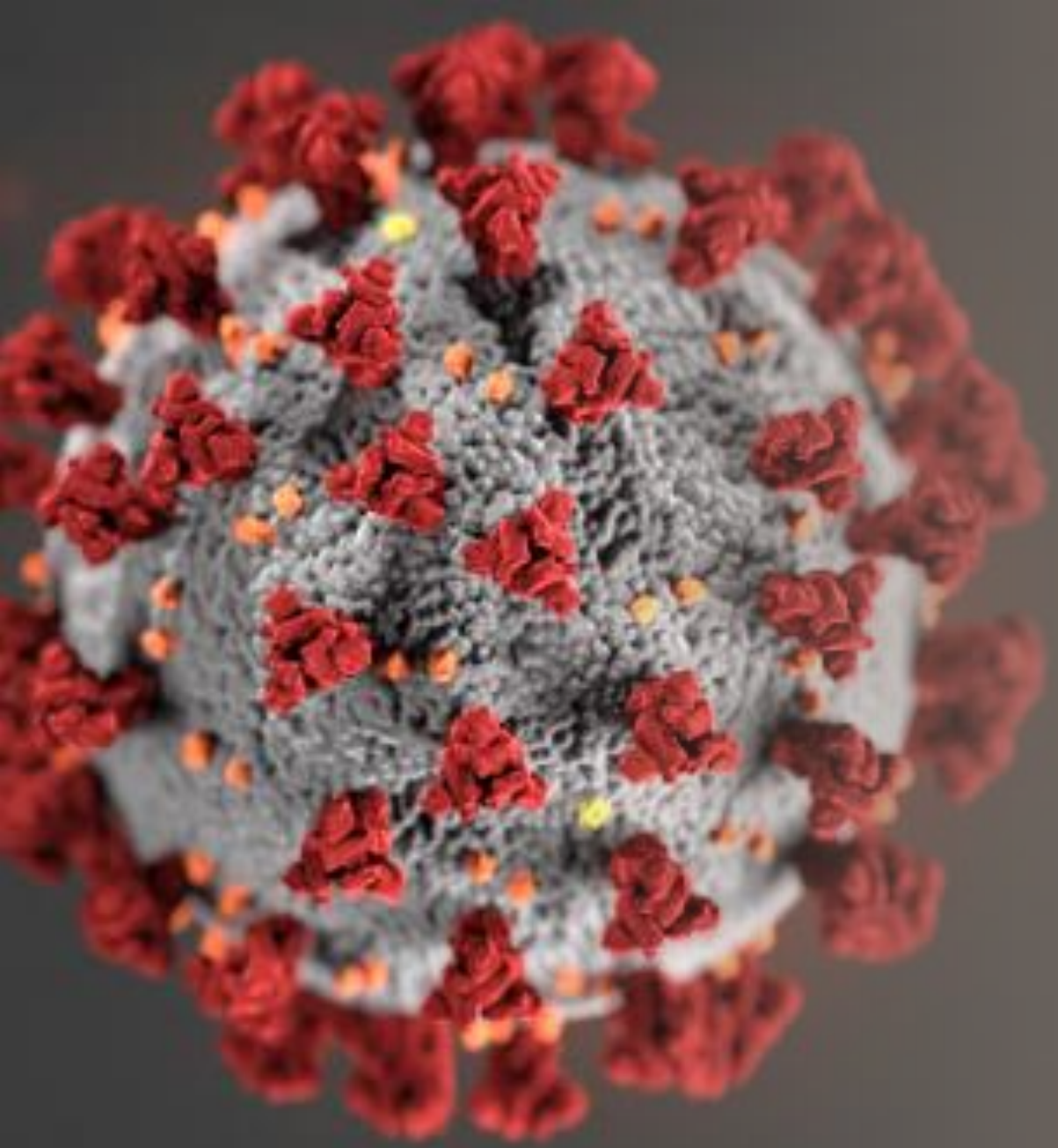
Measures a test's ability to correctly generate a *negative* result for people who *don't* have the condition that's being tested for (also known as the "true negative" rate). A high-specificity test will correctly rule out almost everyone who *doesn't* have the disease and won't generate many false-positive results.

- QFT – 99%
- T-Spot – 85-98%
- TST
  - BCG – 49%
  - No BCG – 97%



# TB Cases and Rates Among U.S.-born versus Non-U.S.–born Persons, United States, 1993–2019





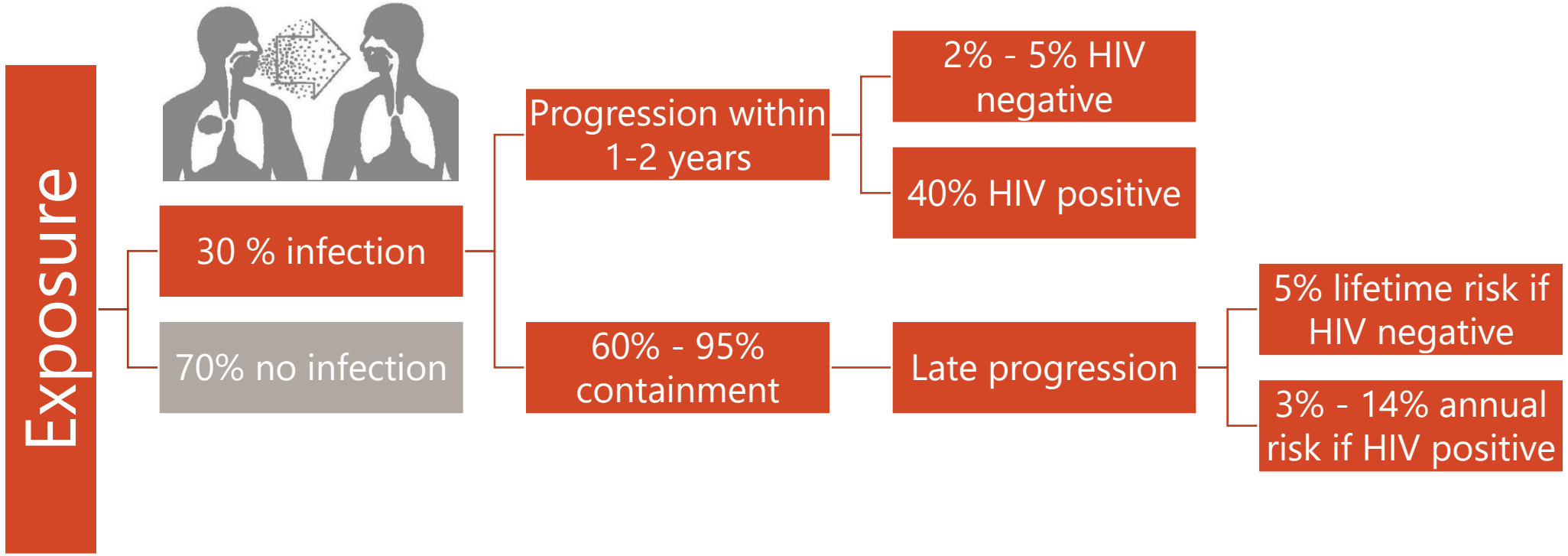
# 2020 U.S. TB Cases

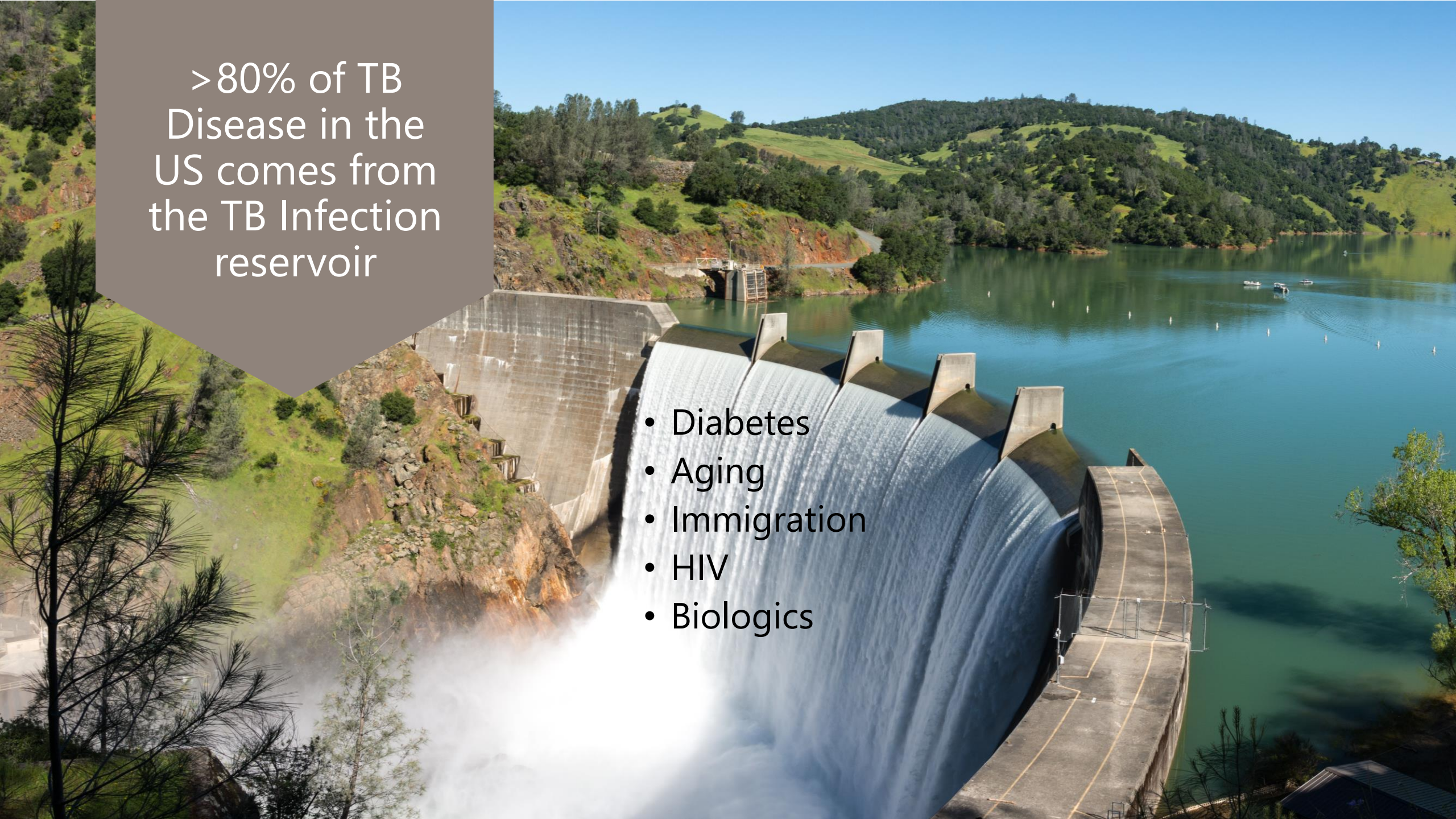
Decrease due to:

- Less new arrivals/international travel
- Missed/Delayed Diagnosis
- Reluctance to Seek Care
- Mask Wearing
- Death due to SARS-CoV-2

# Beware of Data


Are certain individuals at increased risk of progression from TB infection to TB disease?


Exposure
30 % infection
70% no infection
Progression within 1-2 years
60% - 95% containment
2% - 5% HIV negative
40% HIV positive
Late progression
5% lifetime risk if HIV negative
3% - 14% annual risk if HIV positive


>80% of TB Disease in the US comes from the TB Infection reservoir
• Diabetes
• Aging
• Immigration
• HIV
• Biologics

# Risk Factors for TB Activation

Relative risk of TB compared to the general population

## High Risk Factors

| | |
|---|---|
| • HIV/AIDS | 50 - 170 |
| • Close Contact | 15 |
| • Organ-transplant recipients | 20 - 74 |
| • Chronic renal failure requiring dialysis | 10 - 25 |
| • TNF-alpha blockers | 2 - 9 |
| • Silicosis | 3 |

## Moderate Risk Factors

| | |
|---|---|
| • Fibronodular disease on chest x-ray | 6-19 |
| • Immigrants from high TB prevalence countries | 3 - 5 |
| • Diabetes mellitus | 2 – 5 |
| • Use of corticosteroids | 5 |

## Low Risk Factors

| | |
|---|---|
| • Smoking | 2 |
| • Low body weight | 2 – 3 |
| • Healthcare workers | 2.5 |

# Published Studies Show Increased CD8 Responses Among Contacts

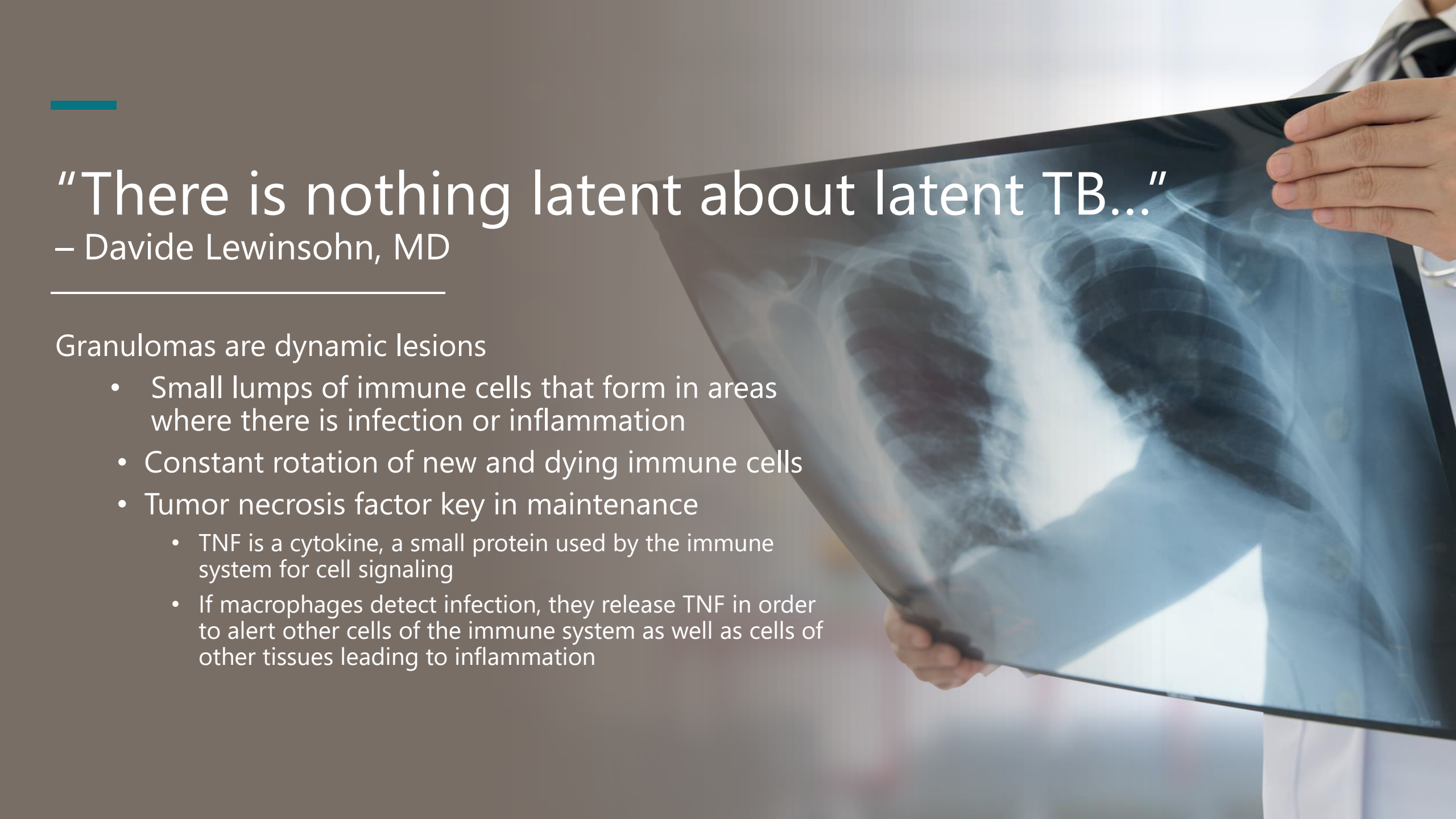
| Contact study | N | Positive by QFT-Plus | | Percent with CD8 signal >0.6 IU/ml TB2–TB1 of QFT-Plus positive results |
|---|---|---|---|---|
| Barcellini, L et al. (2016) ERJ. 48(5):1411–1419 | 119 | 68/119 | 57% | 25% |
| Pieterman, E.D. et al (2018) TB 108, 136–142 | 127 | 54/127 | 42% | 33% |
| Lee, M.R. et al. (2019) J Infect. 78(4):299–304 | 223 | 105/223 | 47% | 13.3% |
| Gurjav, U. et al. (2019) IJTLD. 23(8):919–923 | 189 | 135/280 | 48.2% | 22.6% |

New indicator of recent transmission among contacts?

# “There is nothing latent about latent TB…”
– Davide Lewinsohn, MD

Granulomas are dynamic lesions

- Small lumps of immune cells that form in areas where there is infection or inflammation
- Constant rotation of new and dying immune cells
- Tumor necrosis factor key in maintenance
  - TNF is a cytokine, a small protein used by the immune system for cell signaling
  - If macrophages detect infection, they release TNF in order to alert other cells of the immune system as well as cells of other tissues leading to inflammation



# Primary Care Provider and Nurse Knowledge, Attitudes and Skills regarding LTBI Management

### TBI Screening

Most know some factors that should prompt screening

Majority preferred IGRA to TST

Misconceptions about IGRA such as cost and approved age of person to test

### TB Disease Evaluation

Most were comfortable conducting TB disease evaluation (CXR and symptom screen)

Some mention lack of patient volume

Some noted language as a barrier to evaluate appropriately

### TBI Treatment Initiation, Follow-Up and Completion of Treatment

Most were not confident nor comfortable regarding treatment for TB infection in primary care

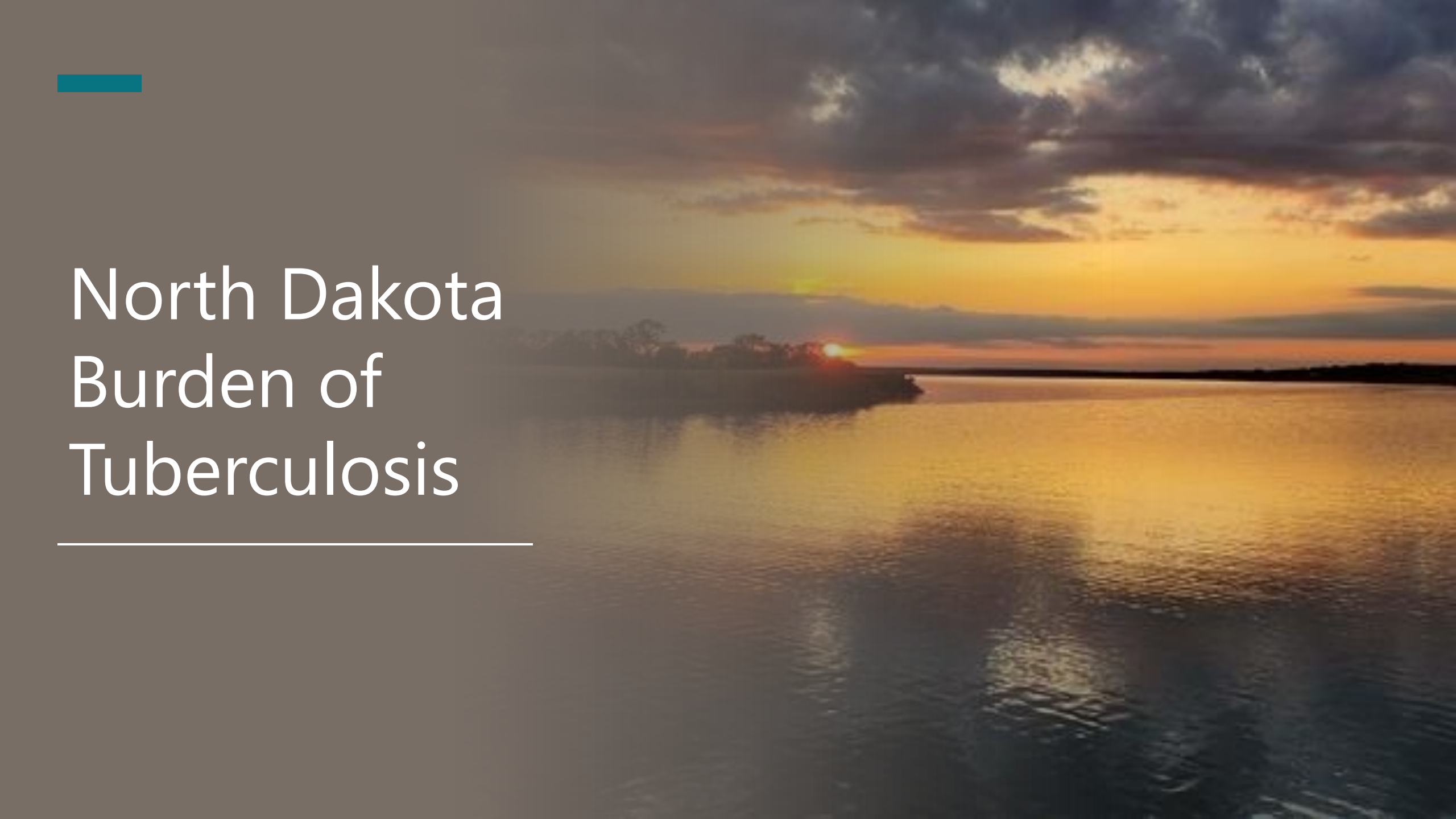
Most could not name the common treatment regimens or duration of treatment

Some mentioned a perception that specialists had more infrastructure to treat and acknowledged ease of referral compared to treating in primary care

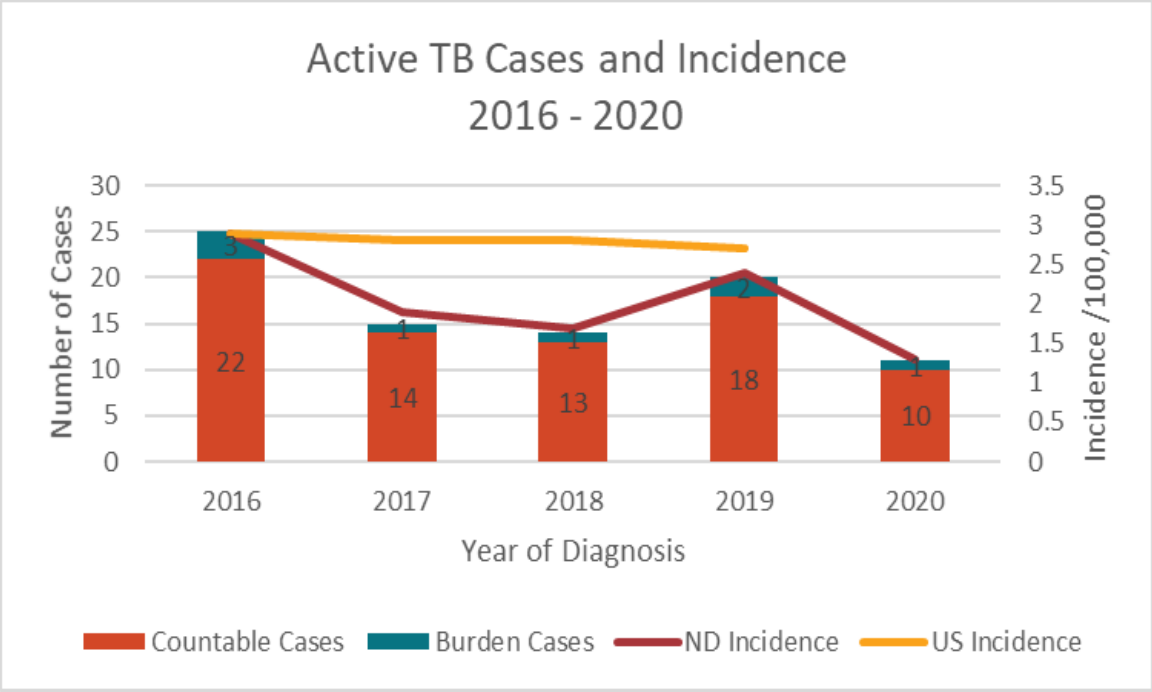

# Cost of TB Treatment

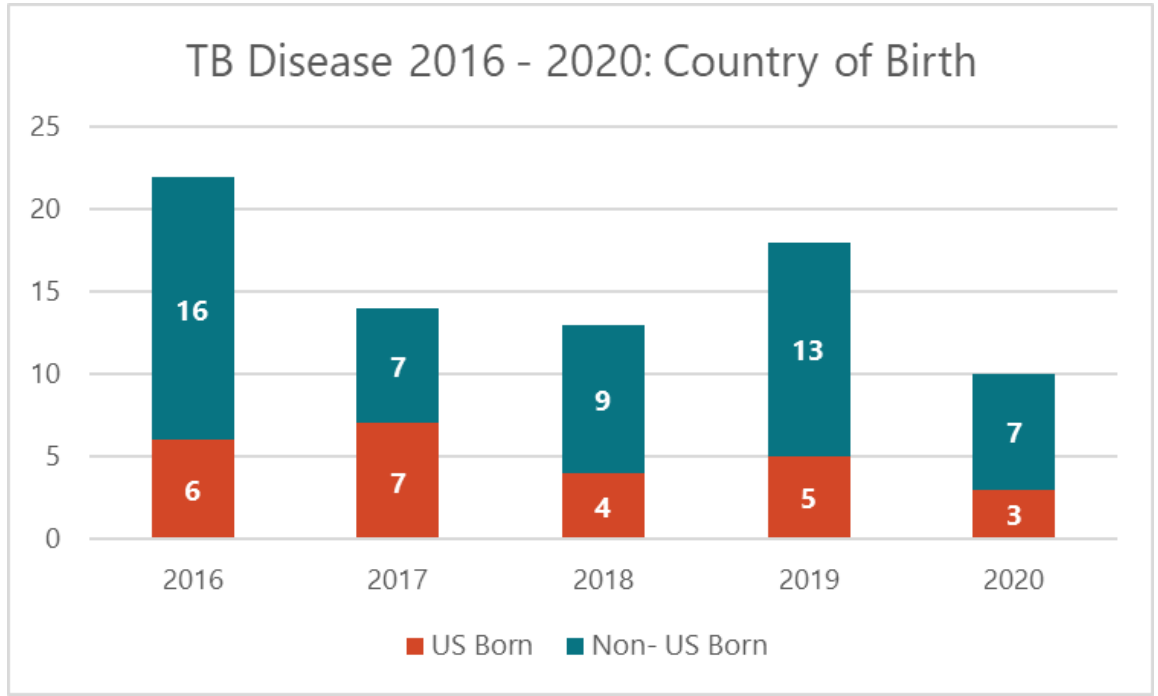
- TB infection $700
- TB Disease $17,000
- MDR-TB $400,000
- XDR-TB >$1,000,000

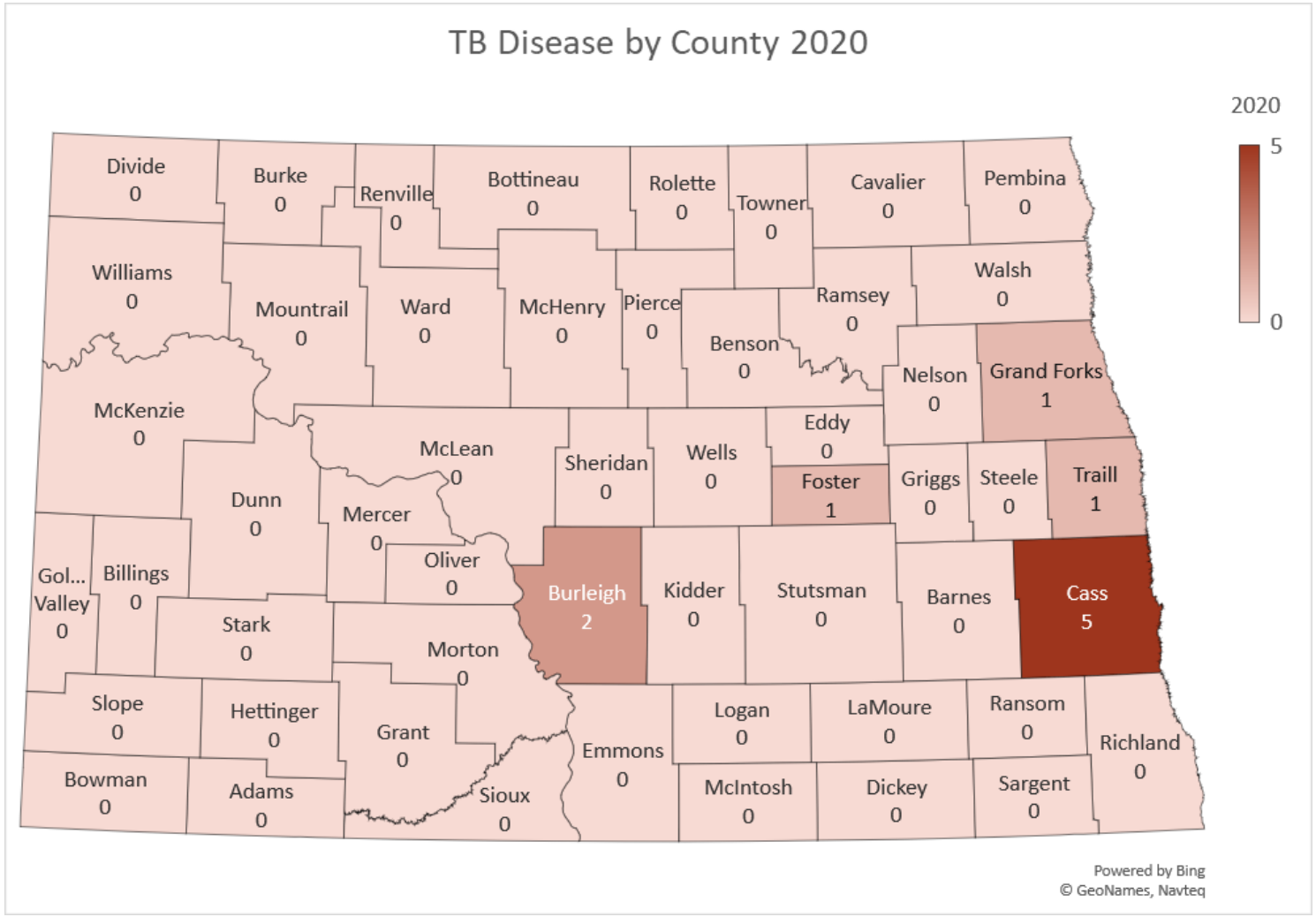
# North Dakota Burden of Tuberculosis



# North Dakota Cases of TB Disease




TB Disease by County 2020
2020
5
0
Divide 0
Burke 0
Renville 0
Bottineau 0
Rolette 0
Towner 0
Cavalier 0
Pembina 0
Williams 0
Mountrail 0
Ward 0
McHenry 0
Pierce 0
Benson 0
Ramsey 0
Walsh 0
Nelson 0
Grand Forks 1
McKenzie 0
McLean 0
Sheridan 0
Wells 0
Eddy 0
Foster 1
Griggs 0
Steele 0
Traill 1
Dunn 0
Mercer 0
Oliver 0
Gol... Valley 0
Billings 0
Stark 0
Burleigh 2
Kidder 0
Stutsman 0
Barnes 0
Cass 5
Morton 0
Slope 0
Hettinger 0
Grant 0
Emmons 0
Logan 0
LaMoure 0
Ransom 0
Richland 0
Bowman 0
Adams 0
Sioux 0
McIntosh 0
Dickey 0
Sargent 0
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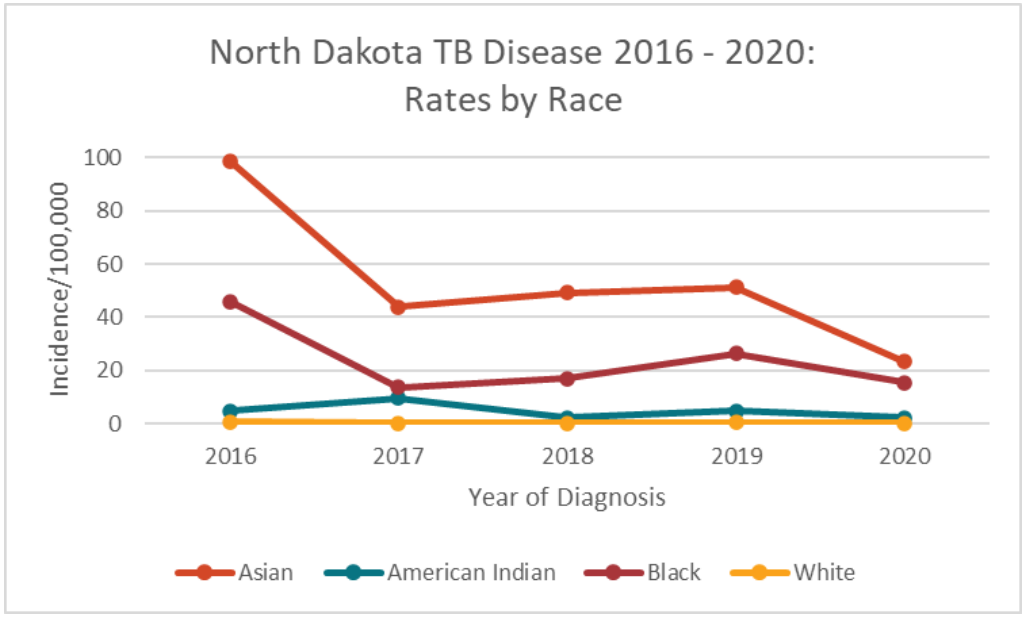
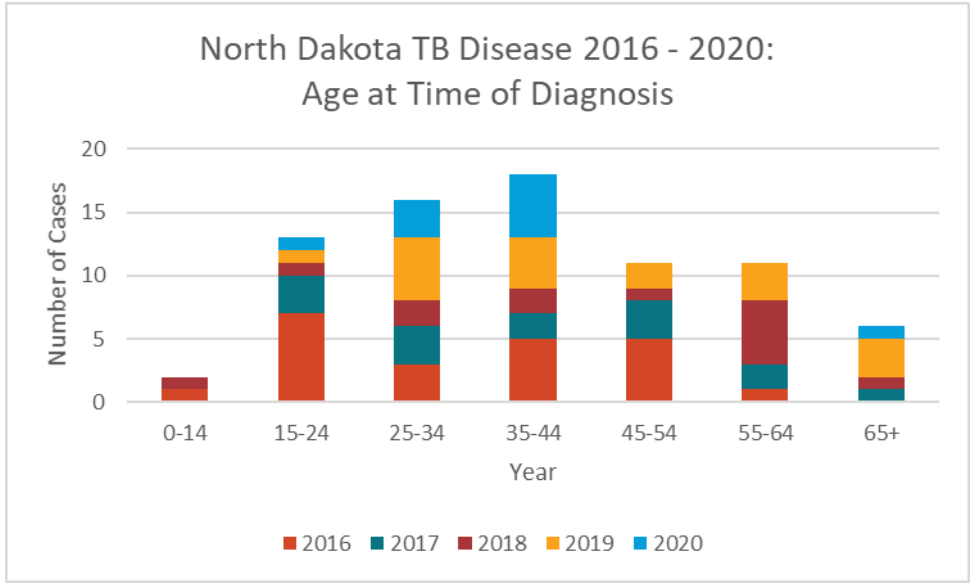
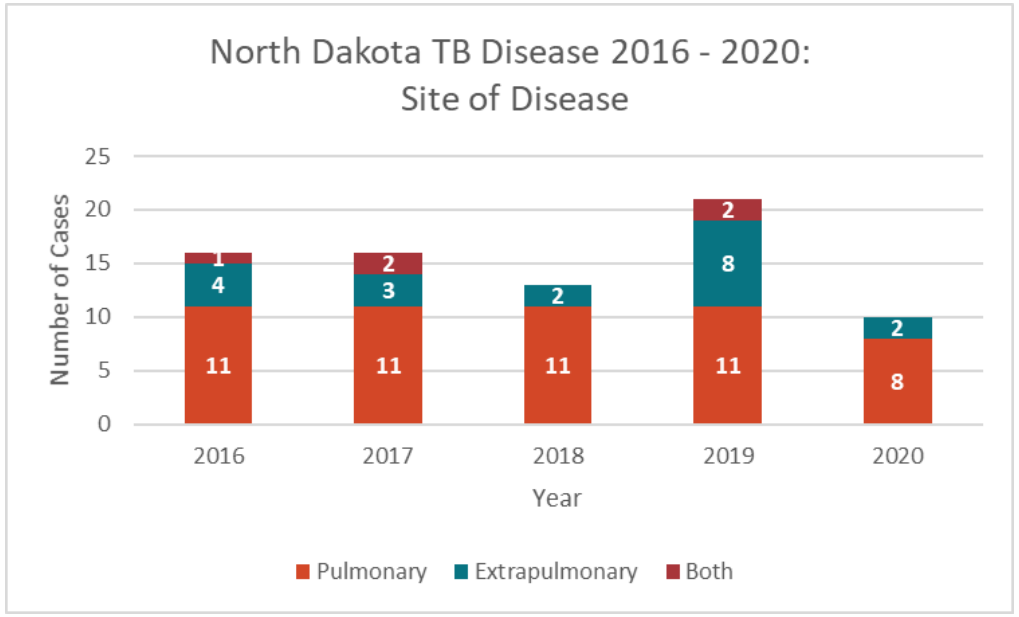
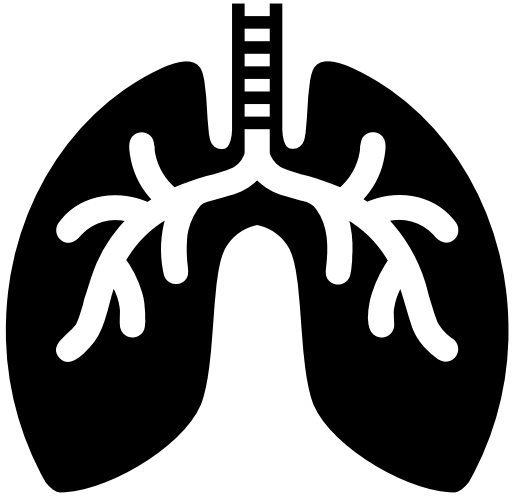
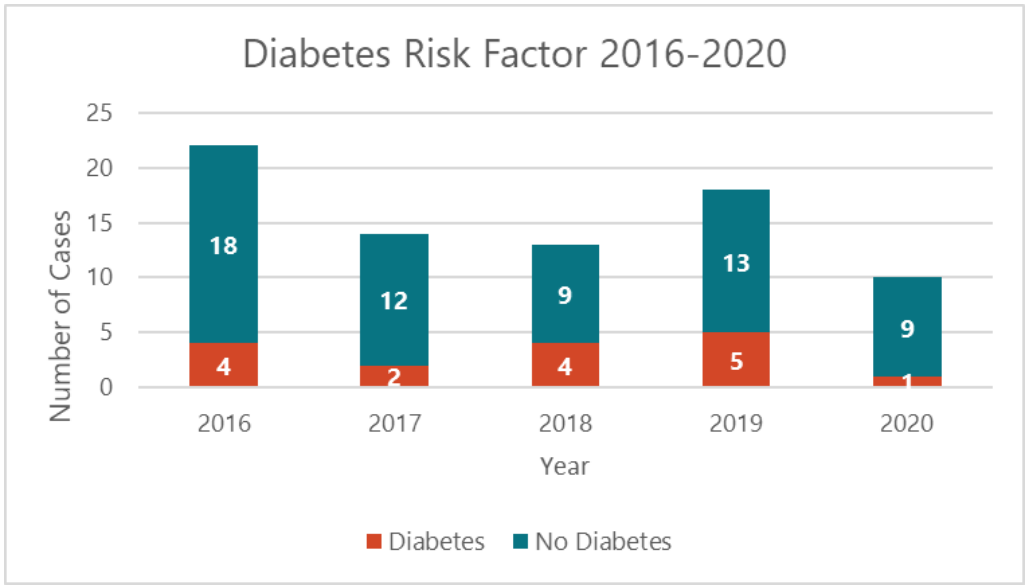

North Dakota TB Disease 2016 - 2020:
Rates by Race
Incidence/100,000
100
80
60
40
20
0
2016
2017
2018
2019
2020
Year of Diagnosis
Asian
American Indian
Black
White

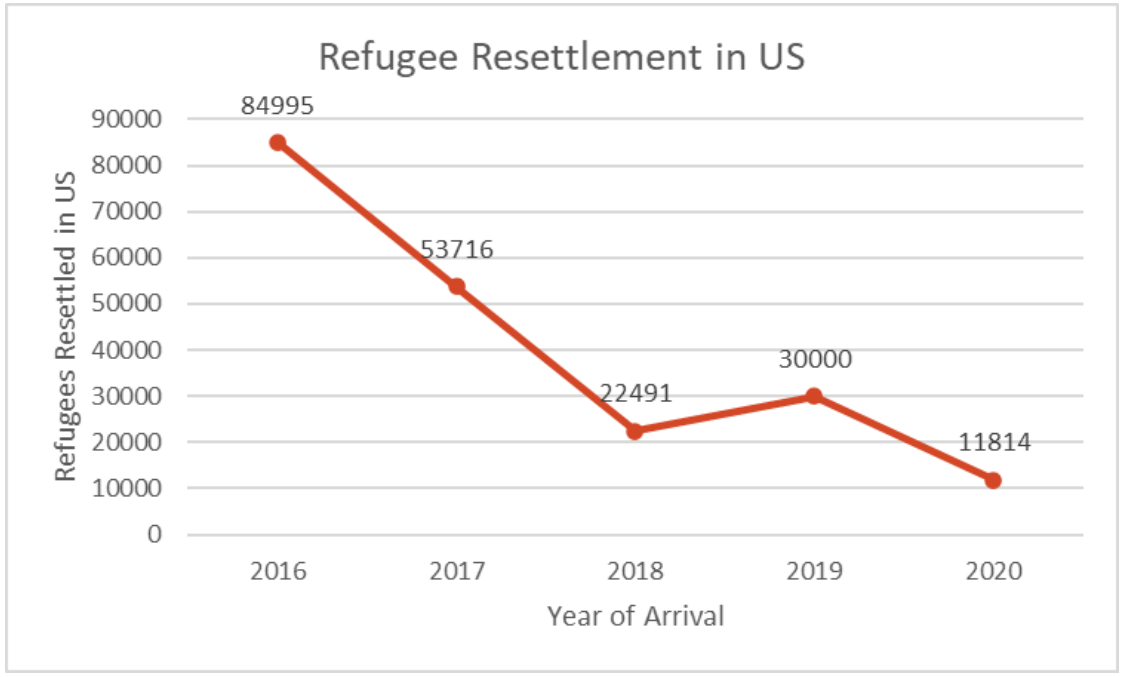

North Dakota TB Disease 2016 - 2020:
Age at Time of Diagnosis
Number of Cases
20
15
10
5
0
0-14
15-24
25-34
35-44
45-54
55-64
65+
Year
2016
2017
2018
2019
2020

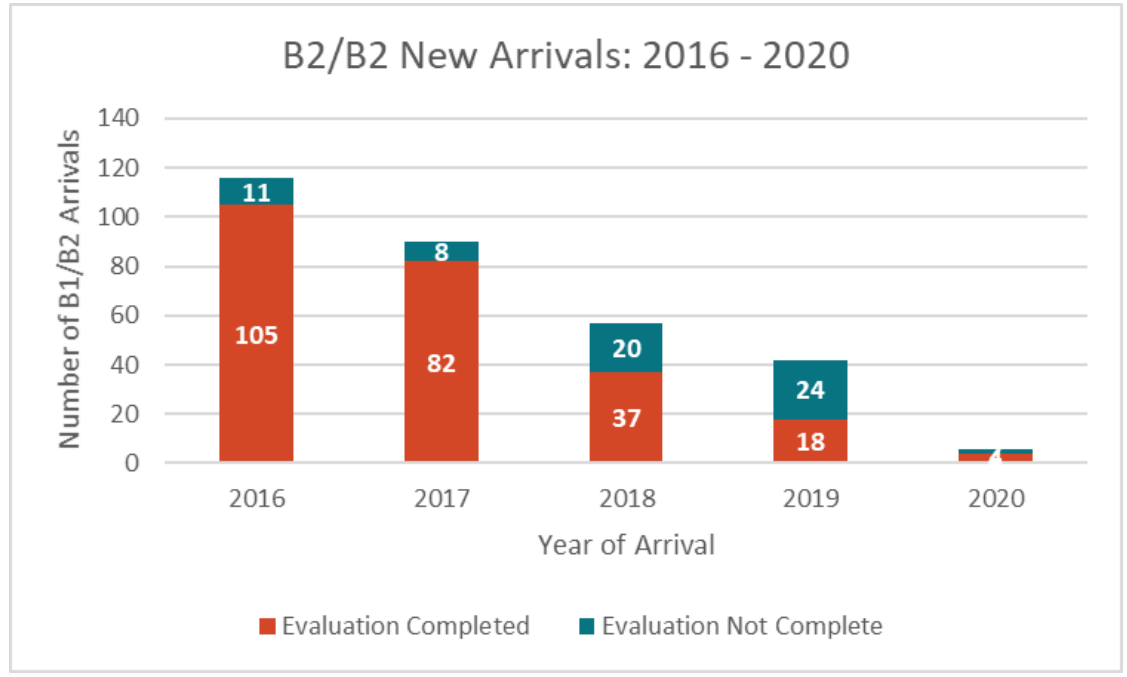

North Dakota TB Disease 2016 - 2020:
Site of Disease
Number of Cases
25
20
15
10
5
0
2016
2017
2018
2019
2020
Year
11
4
1
11
3
2
11
2
11
8
2
8
2
Pulmonary
Extrapulmonary
Both



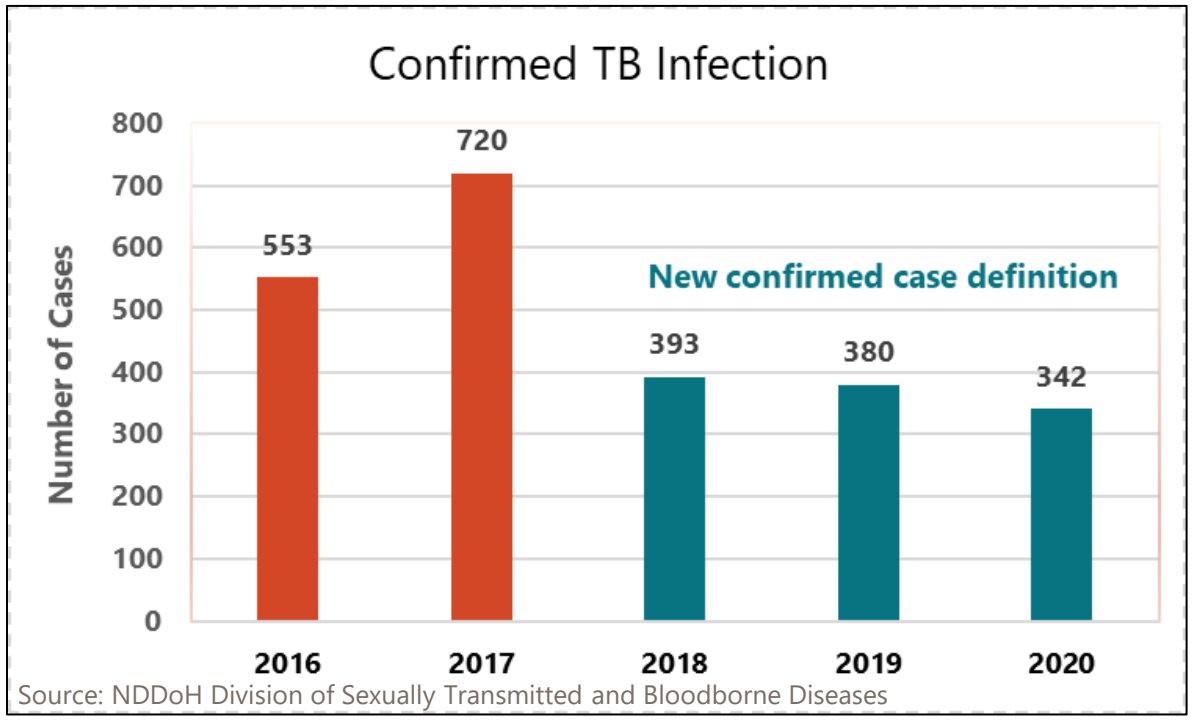

Diabetes Risk Factor 2016-2020
Number of Cases
25
20
15
10
5
0
2016
2017
2018
2019
2020
Year
18
4
12
2
9
4
13
5
9
1
Diabetes
No Diabetes


U.S. Citizenship
and Immigration


Refugee Resettlement in US
Refugees Resettled in US
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
84995
53716
22491
30000
11814
2016
2017
2018
2019
2020
Year of Arrival

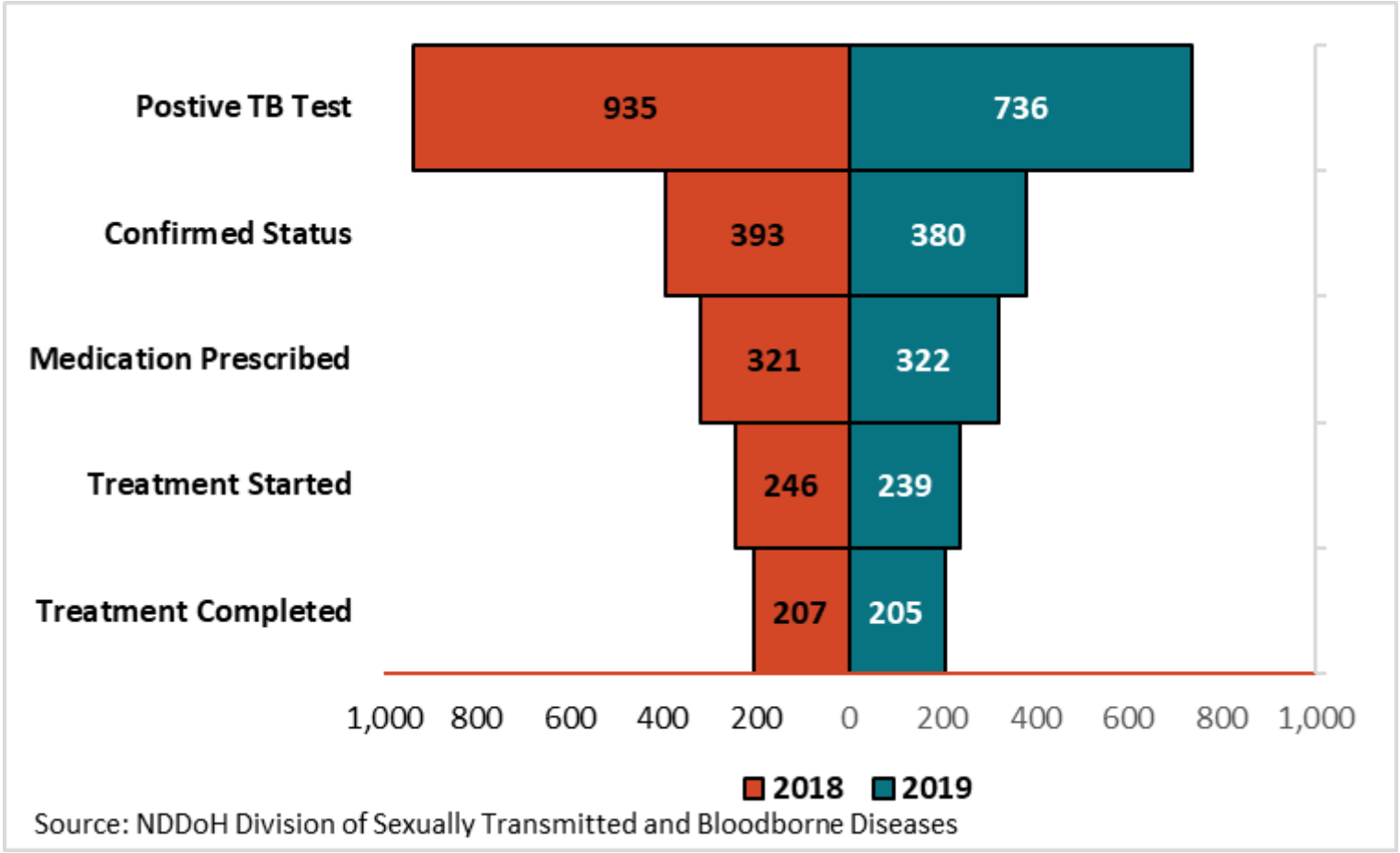

B2/B2 New Arrivals: 2016 - 2020
Number of B1/B2 Arrivals
140
120
100
80
60
40
20
0
11
105
8
82
20
37
24
18
2016
2017
2018
2019
2020
Year of Arrival
Evaluation Completed
Evaluation Not Complete

# TB INFECTION - NORTH DAKOTA



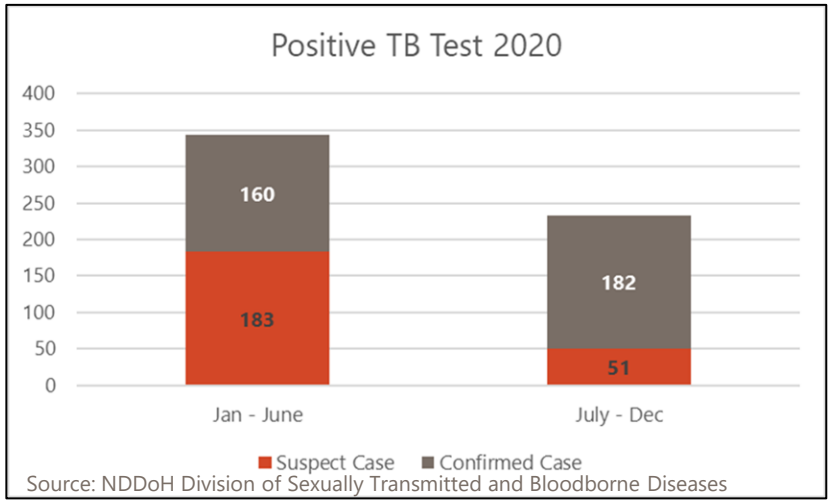

For cases to meet the CSTE case definition, providers must report the laboratory, clinical and radiologic findings as part of the assessment to rule out active TB disease.

# TB INFECTION CASCADE

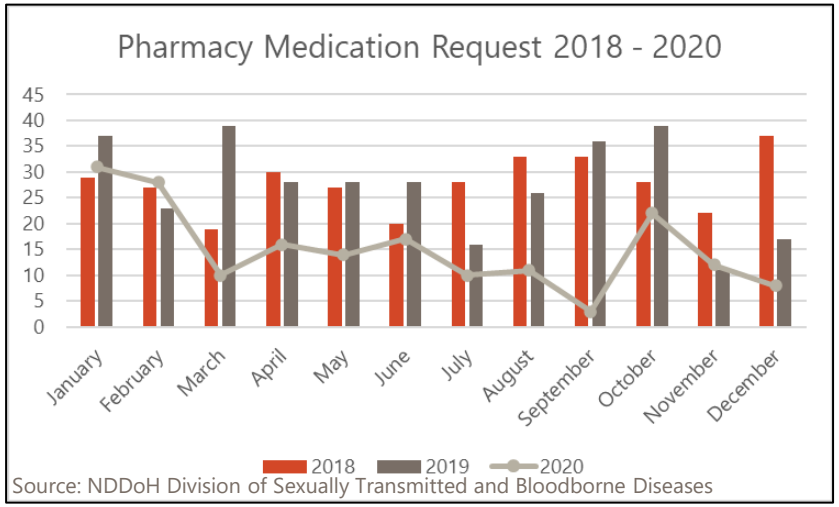


# TB TESTING 2020

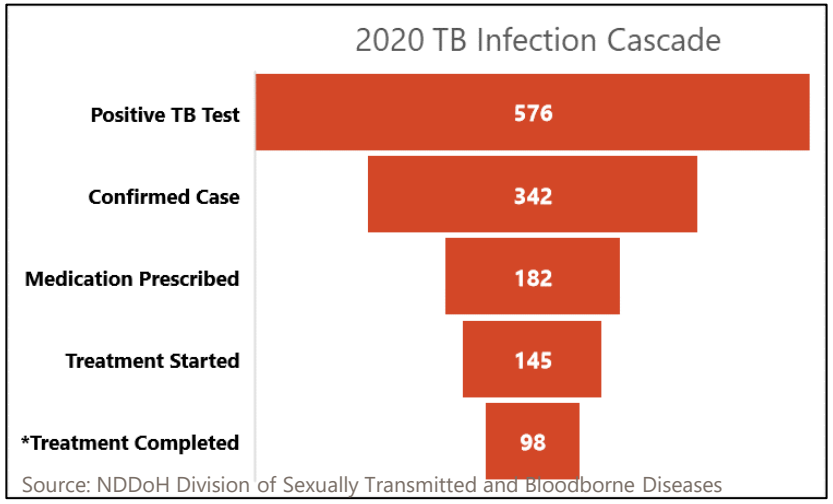
TB Nurse hired the end of June 2020 to follow-up on all positive TB tests reported to NDDoH



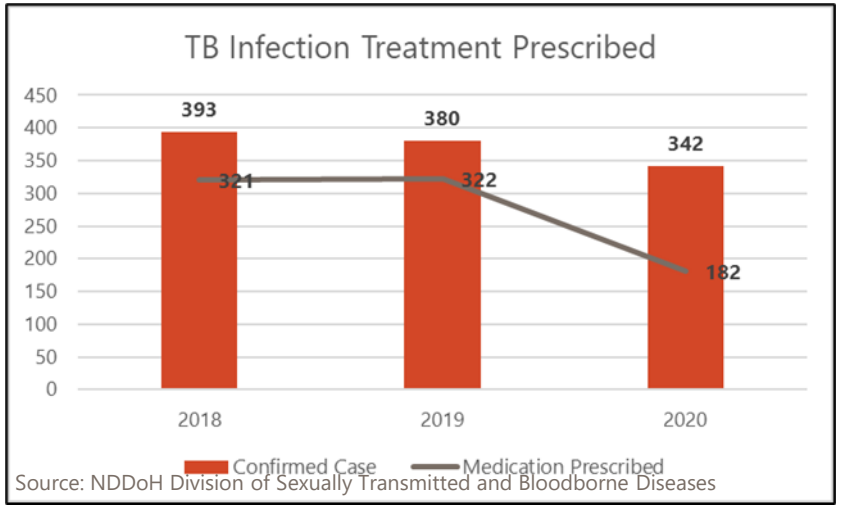
Source: NDDoH Division of Sexually Transmitted and Bloodborne Diseases



Source: NDDoH Division of Sexually Transmitted and Bloodborne Diseases

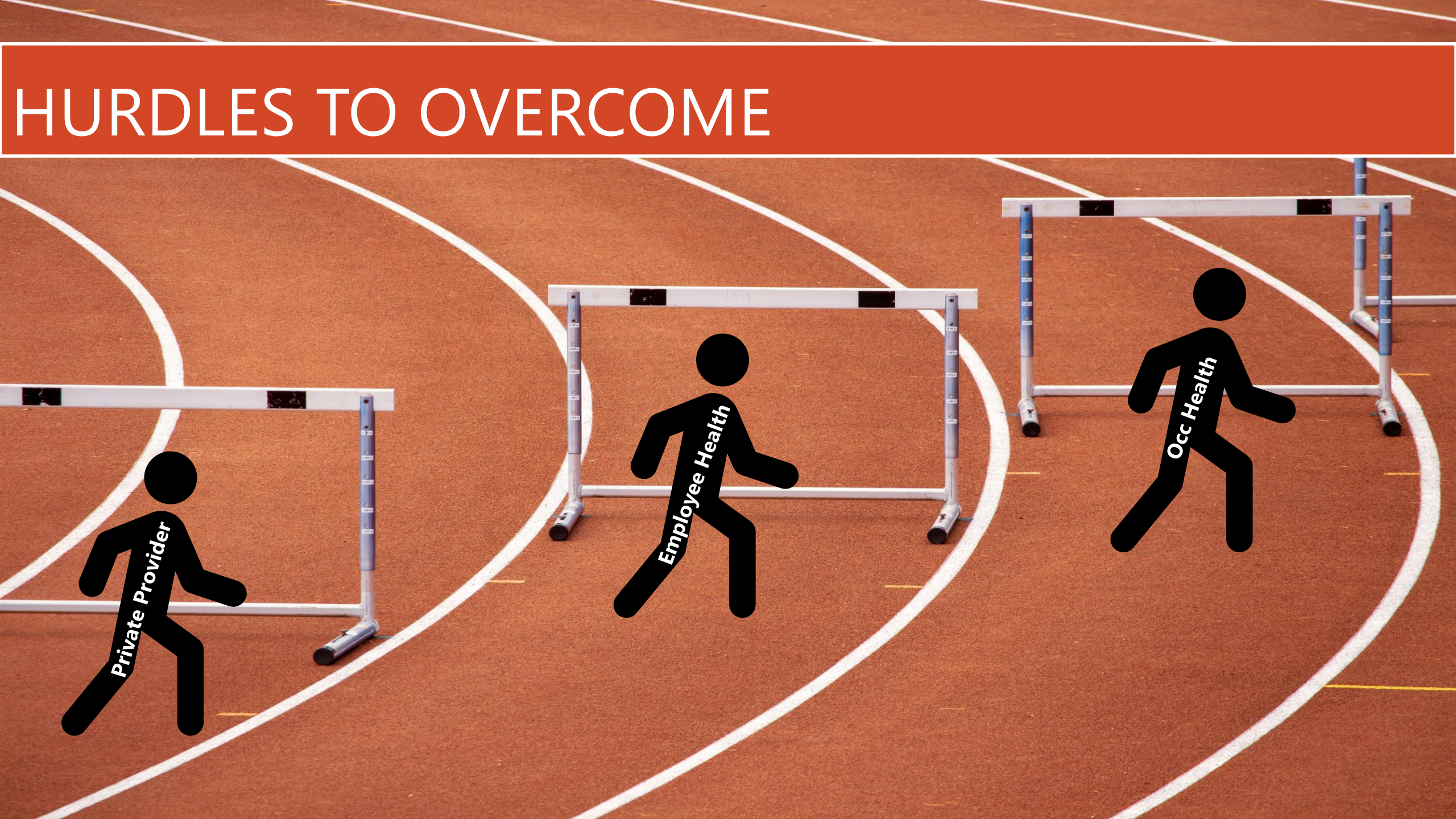


Source: NDDoH Division of Sexually Transmitted and Bloodborne Diseases

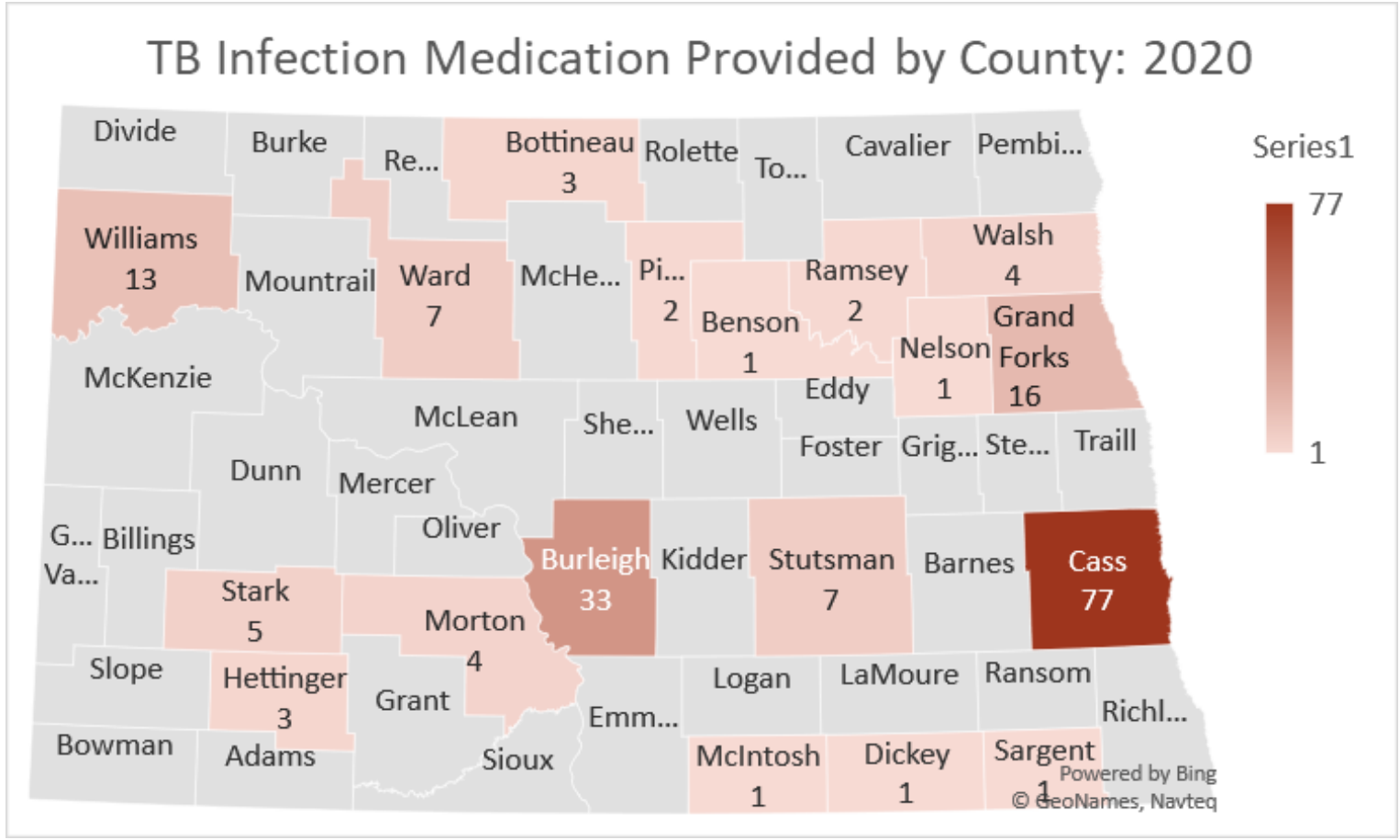


Source: NDDoH Division of Sexually Transmitted and Bloodborne Diseases

# HURDLES TO OVERCOME



# Pharmacy Medication Program



NORTH Dakota | Health
Be Legendary.™

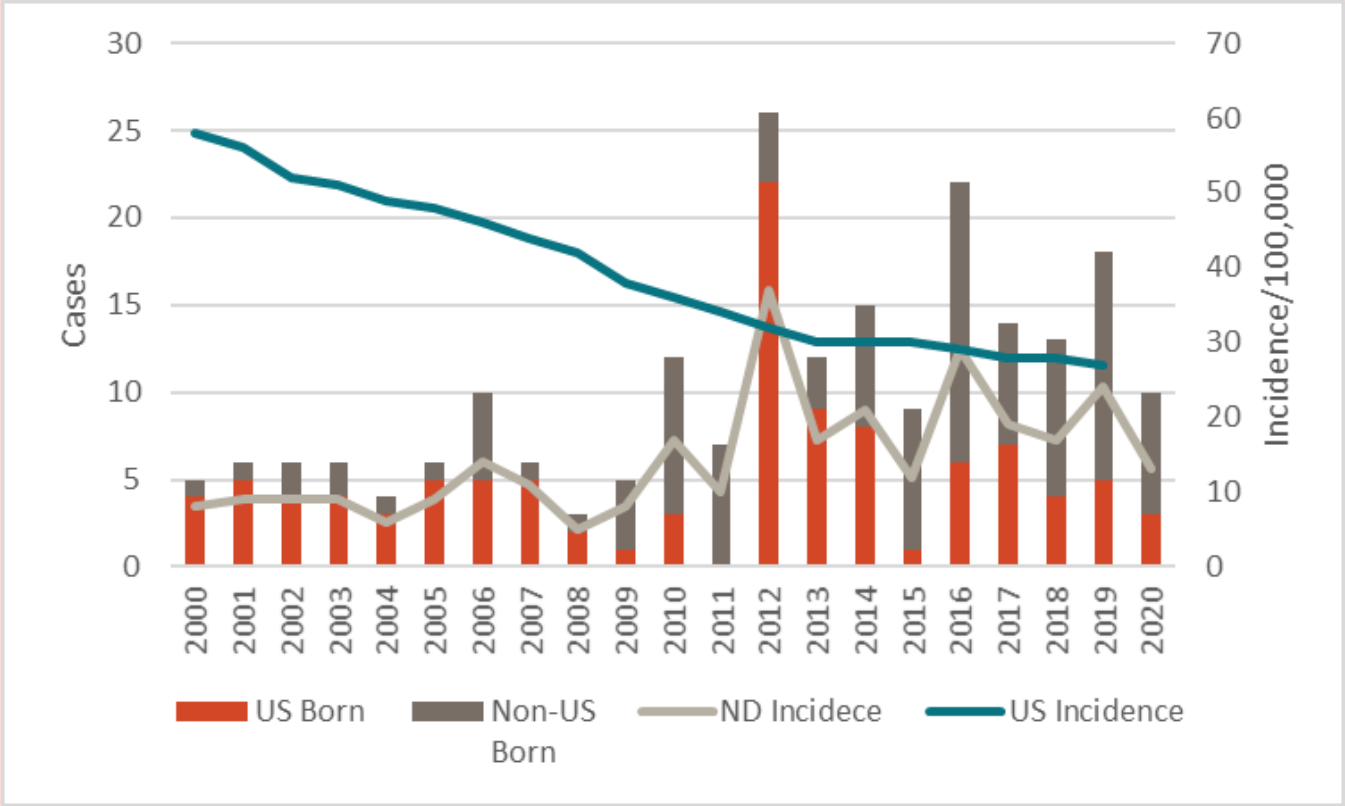
# Tuberculosis Elimination in North Dakota

North Dakota Department of Health
Tuberculosis Elimination Plan (NDTBEP)
December 2020

The World Health Organization defines TB elimination as one (1) TB person diagnosed with active TB per one-million population.

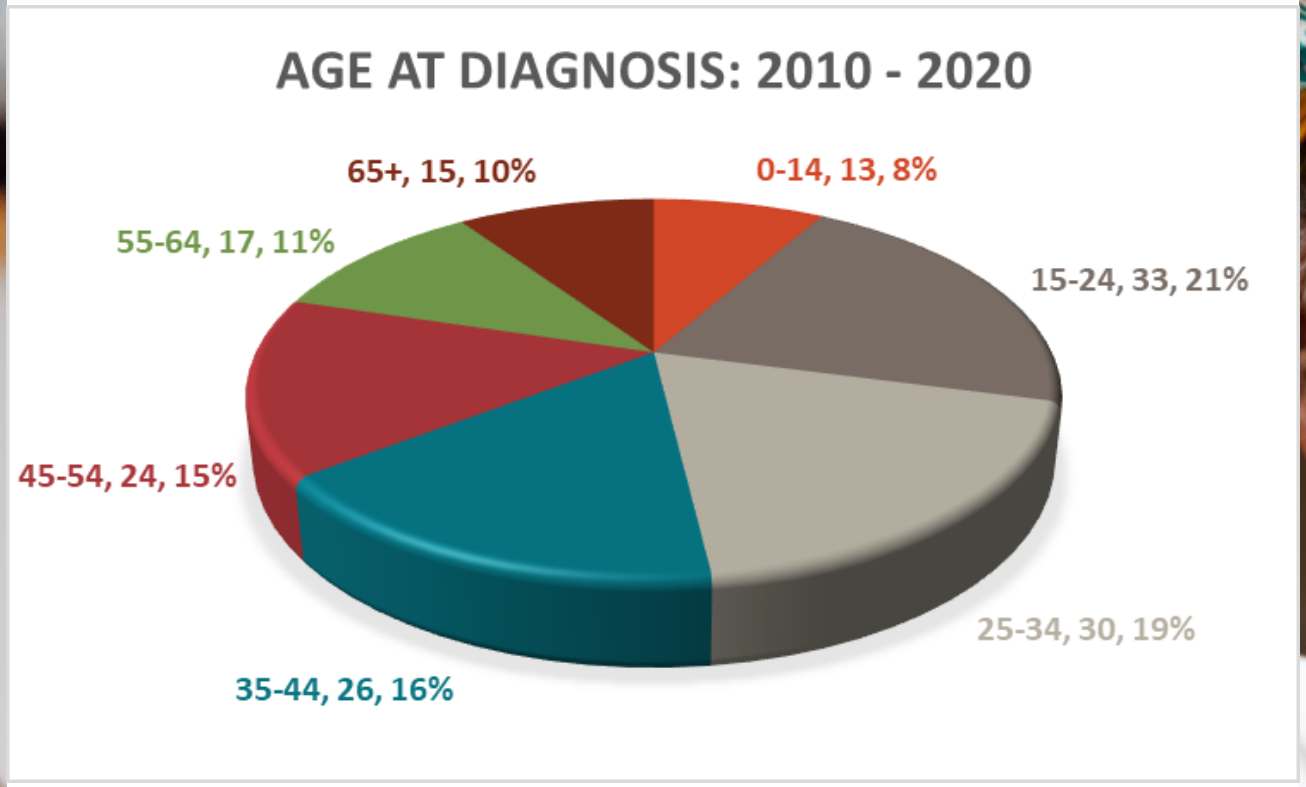
“Pre-elimination” is defined as 10 persons diagnosed with active TB per one-million population.

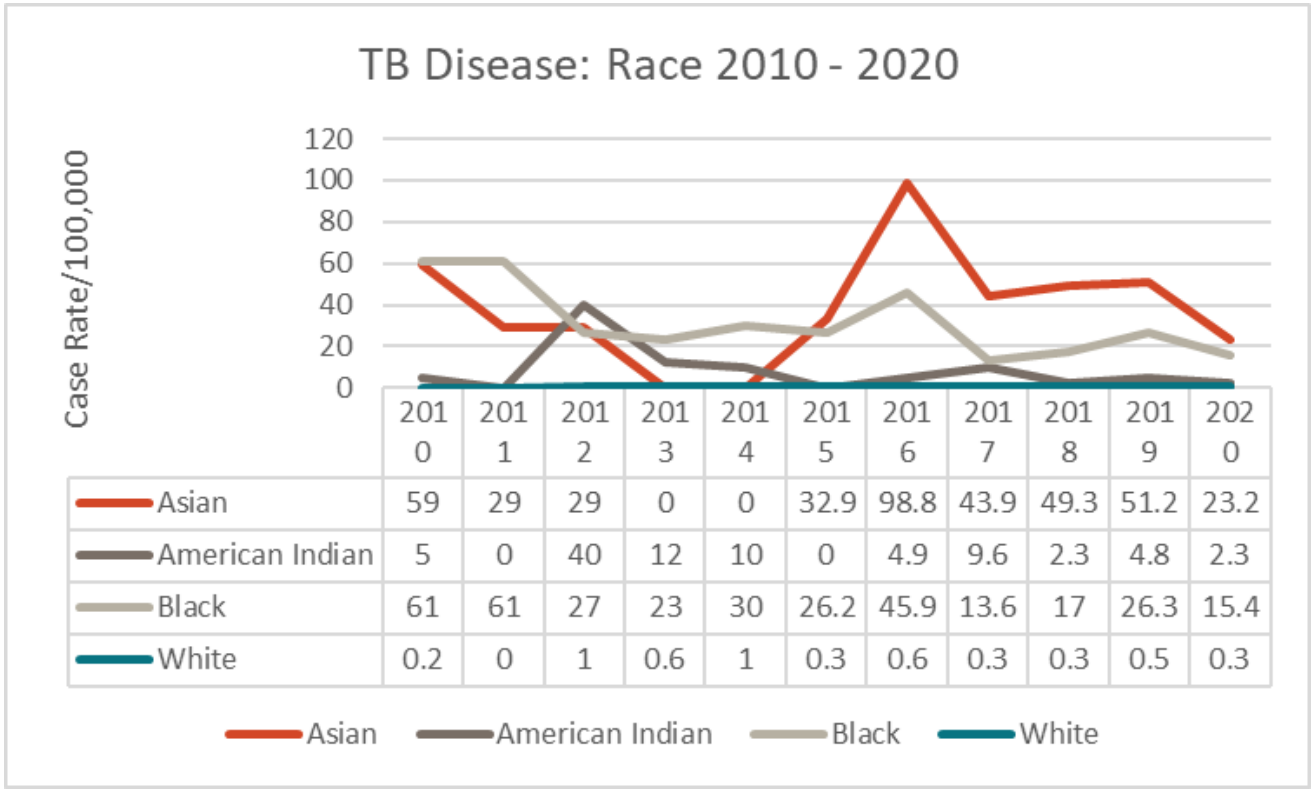
# ACTIVE TB DISEASE: 2000 - 2020

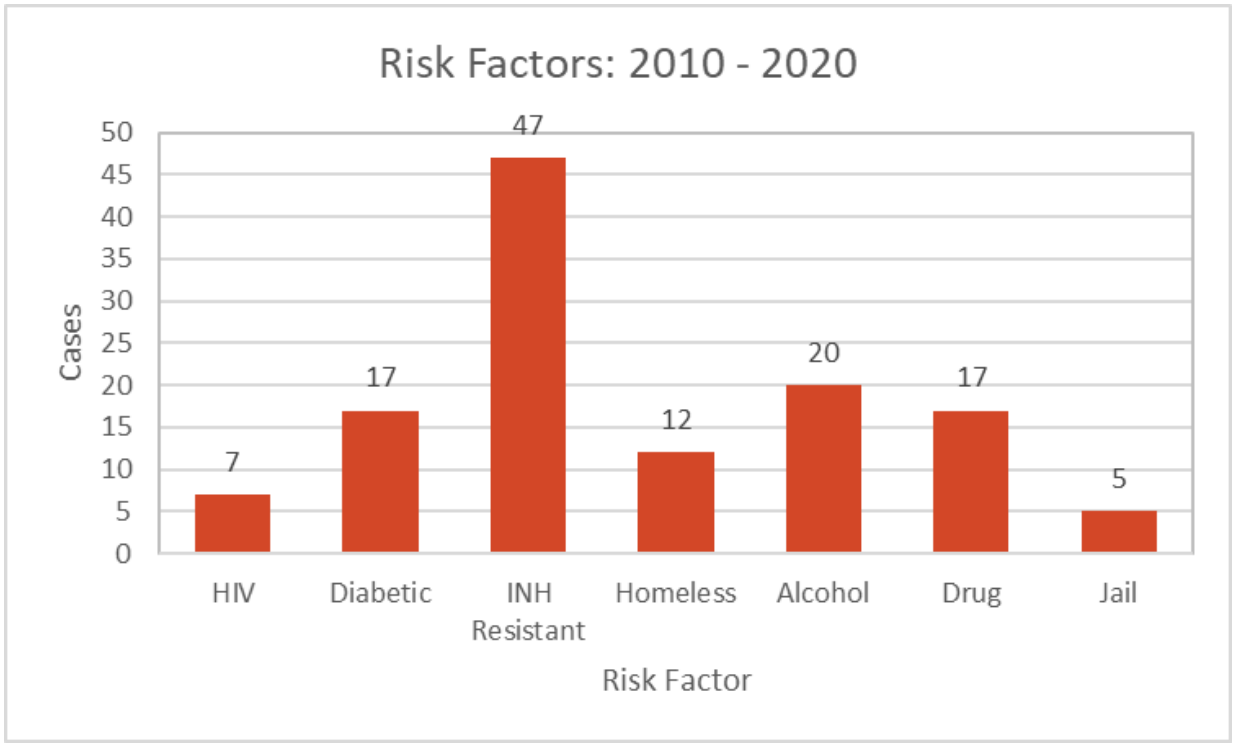


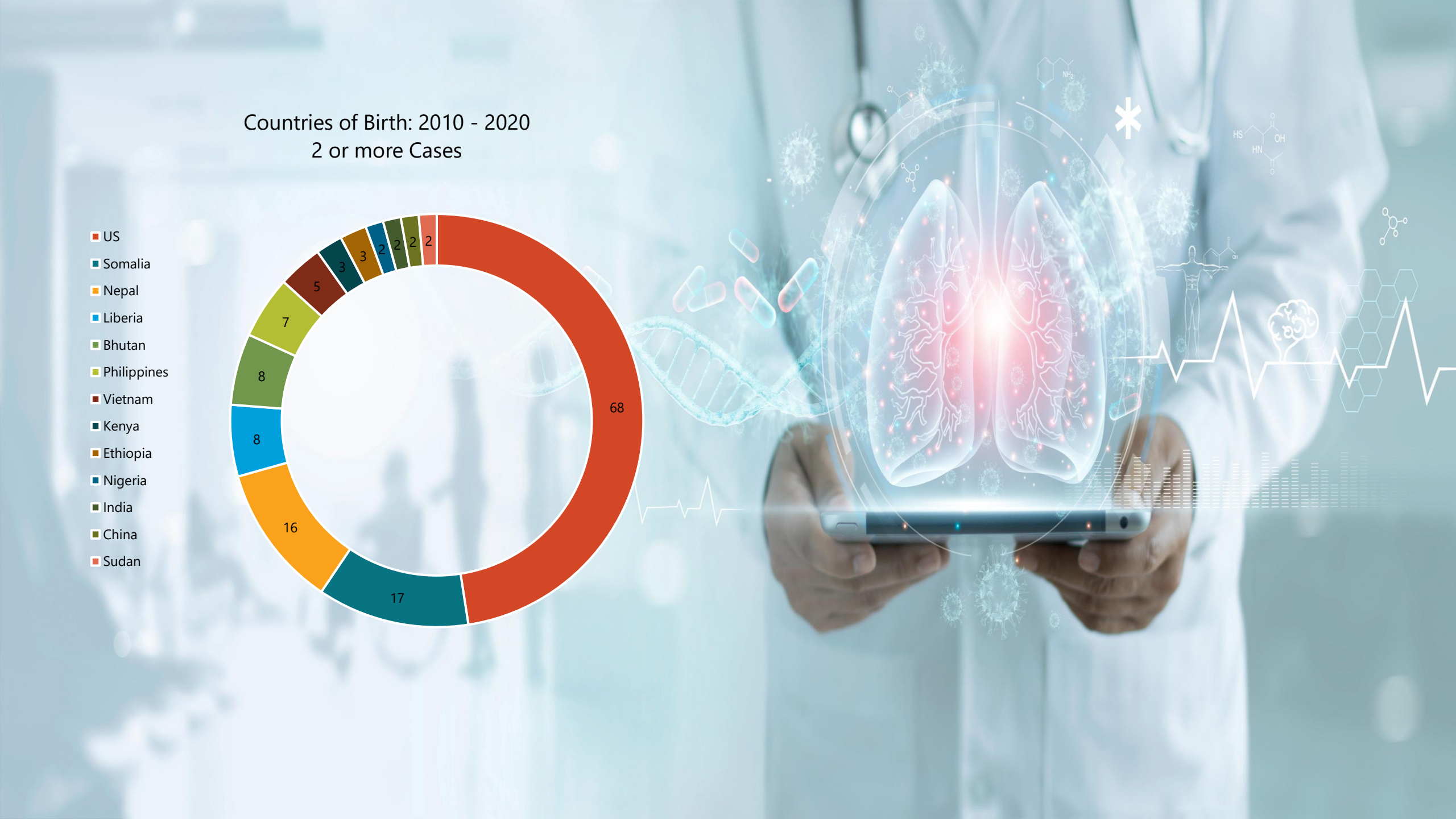

In the years 2000 to 2009, the number of TB persons diagnosed with tuberculosis in North Dakota remained steady with 3-6 persons diagnosed each year with TB disease with a high of 10 persons diagnosed with TB disease in 2006 resulting 57 persons diagnosed and treated for TB disease during that timeframe.

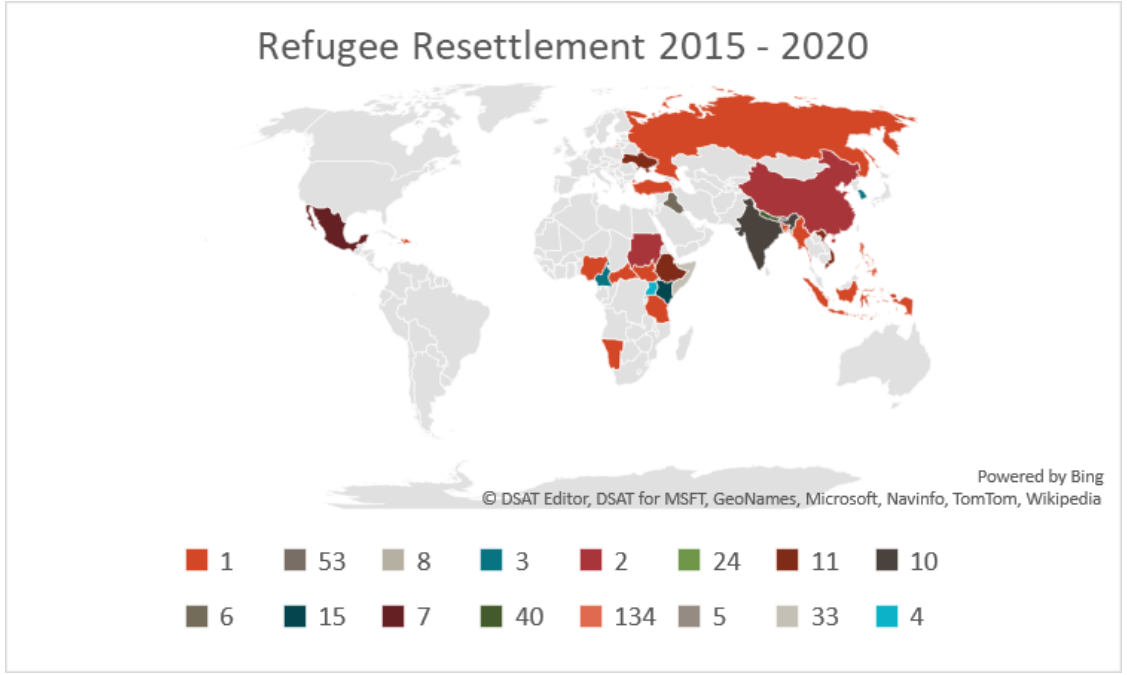
From 2010-2020, the average number of new diagnoses of TB has steadily increased by 160%. During this time period, Grand Forks county experienced a TB outbreak in 2012 which to date has yielded 42 persons with TB disease. The number of persons diagnosed with TB disease range from 7 in 2011 to 26 in 2012 with a total of 158 persons diagnosed and treated for TB disease in North Dakota.

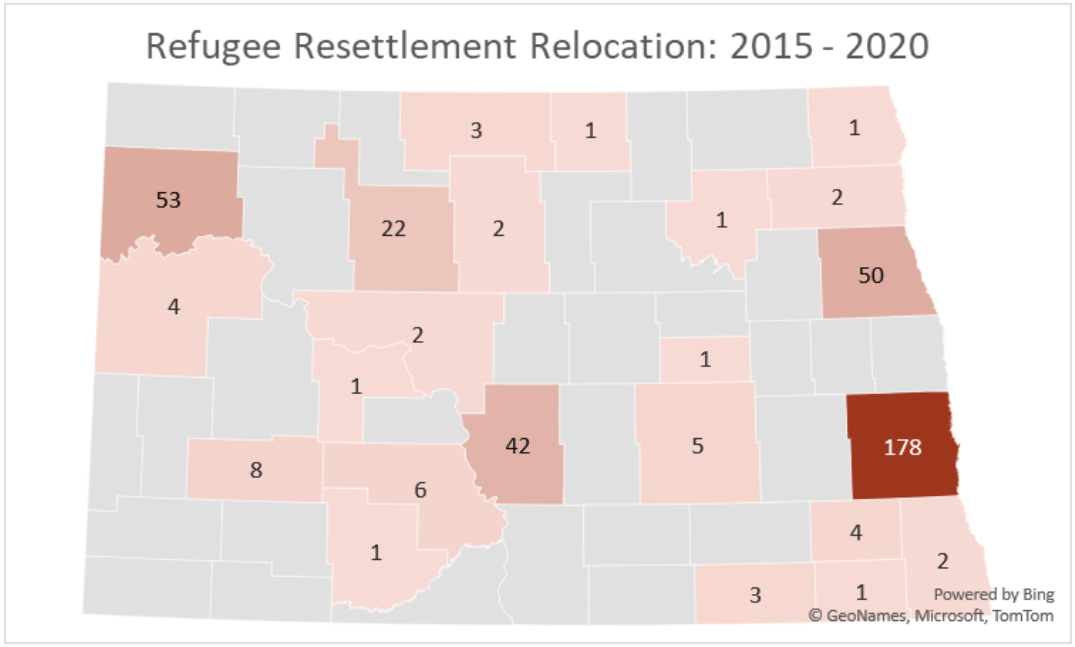

AGE AT DIAGNOSIS: 2010 - 2020
65+, 15, 10%
0-14, 13, 8%
55-64, 17, 11%
15-24, 33, 21%
45-54, 24, 15%
25-34, 30, 19%
35-44, 26, 16%

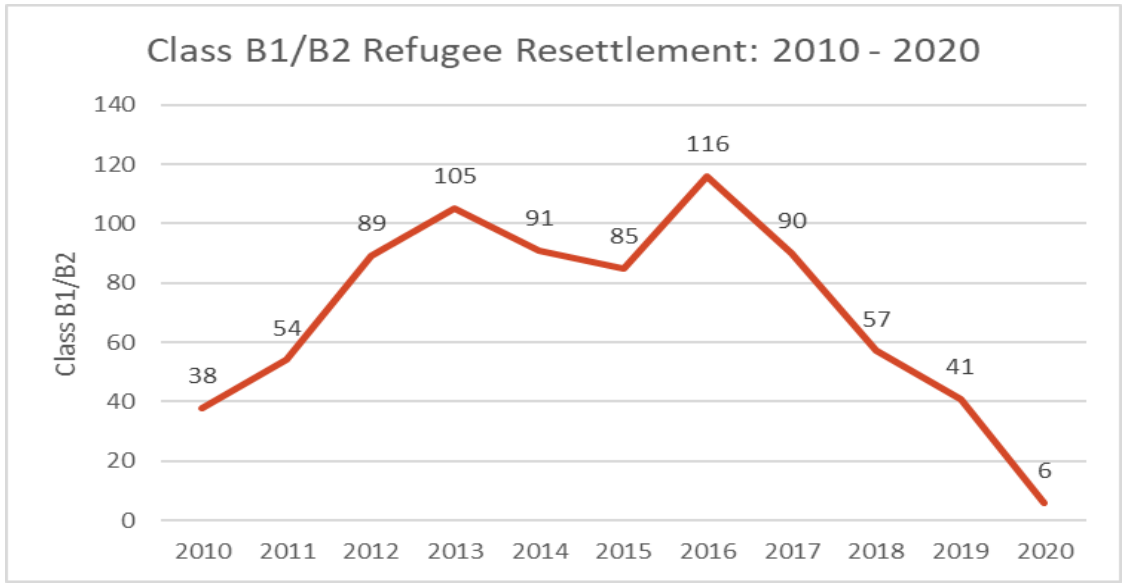

TB Disease: Race 2010 - 2020
Case Rate/100,000
120
100
80
60
40
20
0
2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020
Asian 59 29 29 0 0 32.9 98.8 43.9 49.3 51.2 23.2
American Indian 5 0 40 12 10 0 4.9 9.6 2.3 4.8 2.3
Black 61 61 27 23 30 26.2 45.9 13.6 17 26.3 15.4
White 0.2 0 1 0.6 1 0.3 0.6 0.3 0.3 0.5 0.3
Asian
American Indian
Black
White


Risk Factors: 2010 - 2020
Cases
50
45
40
35
30
25
20
15
10
5
0
7
17
47
12
20
17
5
HIV
Diabetic
INH Resistant
Homeless
Alcohol
Drug
Jail
Risk Factor


Countries of Birth: 2010 - 2020
2 or more Cases
US
Somalia
Nepal
Liberia
Bhutan
Philippines
Vietnam
Kenya
Ethiopia
Nigeria
India
China
Sudan
68
17
16
8
8
7
5
3
3
2
2
2
2

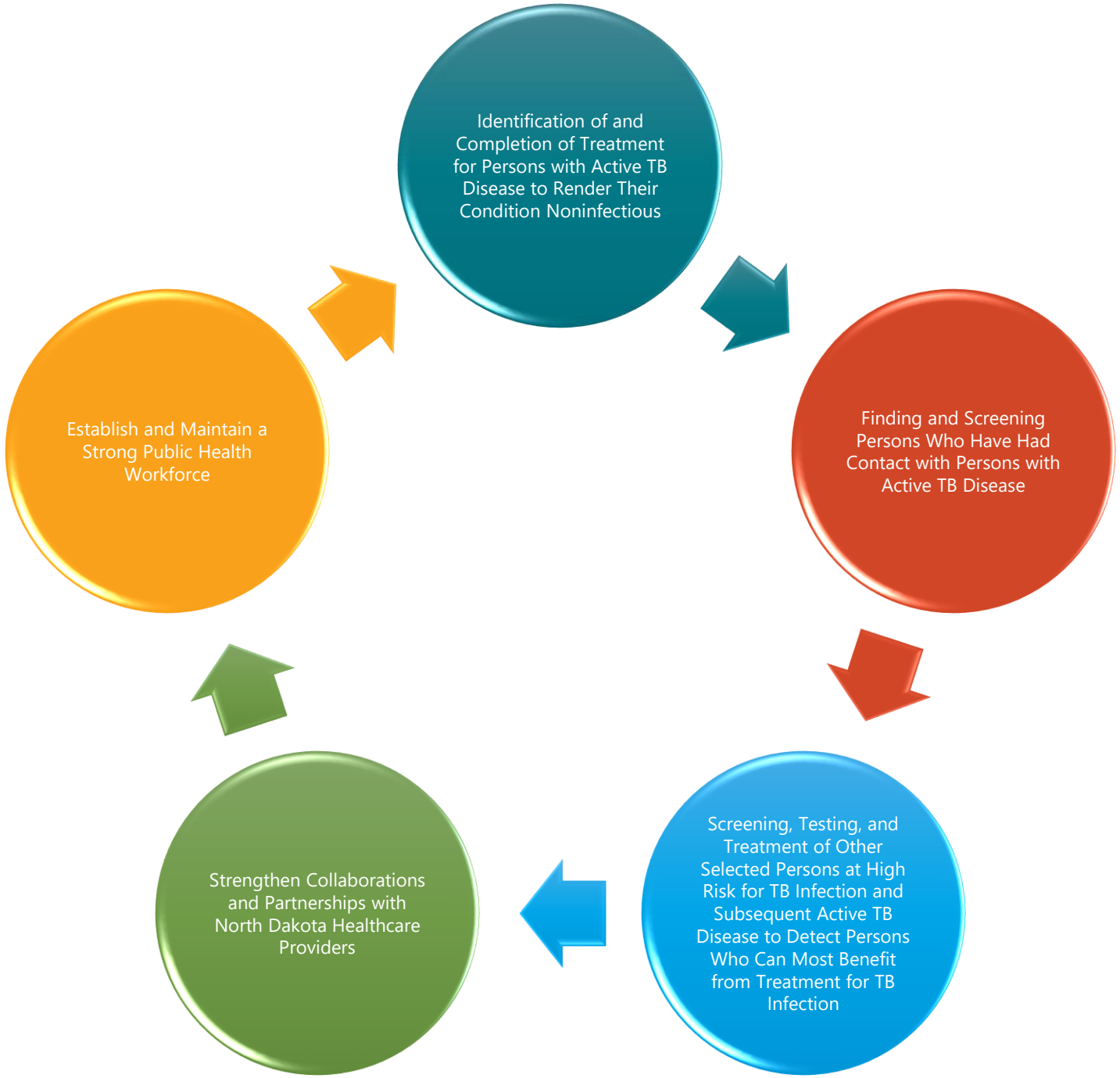



Of 32 countries, 20 countries (66.7%) are designated as high-burden countries for TB, MDR-TB, TB/HIV or a combination of one or more of these categories by the World Health Organization (WHO) for 2016-2020. The following is the breakdown of these countries by WHO designation:

- High burden for TB only: 3.1%
- High burden for MDR-TB only: 6.3%
- High burden for TB/HIV only: 6.3%
- High burden for TB and MDR-TB: 12.5%
- High burden for TB and TB/HIV: 9.4%
- High burden for TB, MDR-TB, and TB/HIV: 25.0%




# ACTION STEPS TO ELIMINATE TB IN ND

# Targets and Indicators Used to Monitor Progress

| Goals for Reducing TB Incidence | | Targets |
|---|---|---|
| TB Incidence | Reduce the incidence of TB disease. | 1.3 cases per 100,000 |
| US-Born Persons | Decrease the incidence of TB disease among US-born persons. | 0.4 cases per 100,000 |
| Non-US–Born Persons | Decrease the incidence of TB disease among non-US–born persons. | 8.8 cases per 100,000 |
| US-Born Non-Hispanic Blacks or African Americans | Decrease the incidence of TB disease among US-born non-Hispanic blacks or African Americans. | 1.0 cases per 100,000 |
| Children Younger than 5 Years of Age | Decrease the incidence of TB disease among children younger than 5 years of age. | 0.1 cases per 100,000 |

| Objectives on Case Management and Treatment | | Targets |
|---|---|---|
| Known HIV Status | Increase the proportion of TB patients with a positive or negative HIV test result reported. | 99% |
| Treatment Initiation | For TB patients with positive acid-fast bacillus (AFB) sputum-smear results, increase the proportion who initiated treatment within 7 days of specimen collection. | 96% |
| Recommended Initial Therapy | For patients whose diagnosis is likely to be TB disease, increase the proportion who start on the recommended initial 4-drug regimen. | 97% |
| Sputum Culture Result Reported | For TB patients aged 12 years or older with a pleural or respiratory site of disease, increase the proportion who have a sputum culture result reported. | 99% |
| Sputum Culture Conversion | For TB patients with positive sputum culture results, increase the proportion with a documented conversion to negative results within 60 days of treatment initiation. | 83% |
| Completion of Treatment | For patients with newly diagnosed TB disease for whom 12 months or less of treatment is indicated, increase the proportion who complete treatment within 12 months. | 95% |

| Objectives on Laboratory Reporting | | Targets |
|---|---|---|
| Turnaround Time — Culture | For TB patients with cultures of respiratory specimens identified with *M. tuberculosis* complex (MTBC), increase the proportion reported by the laboratory within 25 days from the date the specimen was collected. **NOTE:** *25 days includes 21 days for culture to grow and 4 days for specimen collection and delivery to lab.* | 78% |
| Turnaround Time — Nucleic Acid Amplification Test (NAAT) | For TB patients with respiratory specimens positive for MTBC by nucleic acid amplification test (NAAT), increase the proportion reported by the laboratory within 6 days from the date the specimen was collected. NOTE**:** *6 days includes 2 days for detection and 4 days for specimen collection and delivery to lab.* | 97% |
| Drug-Susceptibility Result | For TB patients with positive culture results, increase the proportion who have initial drug-susceptibility results reported. | 100% |
| Universal Genotyping | For TB patients with a positive culture result, increase the proportion who have a MTBC genotyping result reported. | 100% |

| Objectives on Contact Investigations | | Targets |
|---|---|---|
| Contact Elicitation | For TB patients with positive AFB sputum-smear results, increase the proportion who have contacts elicited. | 100% |
| Examination | For contacts to sputum AFB smear-positive TB cases, increase the proportion who are examined for infection and disease. | 94% |
| Treatment Initiation | For contacts to sputum AFB smear-positive TB cases diagnosed with latent TB infection, increase the proportion who start treatment. | 92% |
| Treatment Completion | For contacts to sputum AFB smear-positive TB cases who have started treatment for latent TB infection, increase the proportion who complete treatment. | 93% |

| Objectives on Examination of Immigrants and Refugees | | |
|---|---|---|
| Examination Initiation | For immigrants and refugees with abnormal chest radiographs (X-rays) read overseas as consistent with TB, increase the proportion who initiate a medical examination within 30 days of notification. | 72% |
| Examination Completion | For immigrants and refugees with abnormal chest X-rays read overseas as consistent with TB, increase the proportion who complete a medical examination within 120 days of notification. | 78% |
| Treatment Initiation | For immigrants and refugees with abnormal chest X-rays read overseas as consistent with TB who are diagnosed with latent TB infection or have radiographic findings consistent with prior pulmonary TB (ATS/CDC Class 4) on the basis of examination in the United States, for whom treatment was recommended, increase the proportion who start treatment. | 87% |
| Treatment Completion | For immigrants and refugees with abnormal chest X-rays read overseas as consistent with TB who are diagnosed with latent TB infection or have radiographic findings consistent with prior pulmonary TB (ATS/CDC Class 4) on the basis of examination in the United States, and who have started on treatment, increase the proportion who complete treatment. | 87% |

| Objectives on Data Reporting | | Targets |
|---|---|---|
| RVCT | Ensure the completeness of each core Report of Verified Case of Tuberculosis (RVCT) data item reported to CDC. | 100% |
| ARPE | Ensure the completeness of each core Aggregate Reports for Tuberculosis Program Evaluation (ARPE) data items reported to CDC. | 100% |
| EDN | Ensure the completeness of each core TB Follow-Up Worksheet data item reported to CDC via the Electronic Disease Notification (EDN) system. | 93% |

| Objectives on Program Evaluation | | Targets |
|---|---|---|
| Evaluation Activities | Ensure submission of a program-specific performance-monitoring plan and an annual program evaluation plan to improve program performance. | 100% |
| Evaluation Focal Point | Ensure designation of a TB evaluation focal point. | 100% |

| Objectives on Human Resource Development | | Targets |
|---|---|---|
| Development Plan | Ensure submission of a program-specific human resource development plan (HRD) and a yearly update of progress. | 100% |
| Training Focal Point | Ensure designation of a TB training focal point. | 100% |

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